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THESIS FOR THE DEGREE

OF

M. D.

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THE EPIDEMIOLOGY OF BRONCHIAL CARCINOMA

A description and follow-up of all the cases diagnosed in the area of The Blackburn H.M.C. during 1955, together with comparative figures from the literature and a review of present theories of causation.

by

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Hospital Management Committee.

THIS IS TO CERTIFY

that this Thesis is entirely my own work and composition.

5·8·57

Randal Stalker.

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EPIDEMIOLOGY OF LUNG CANCER

CHAPTER 1

INTRODUCTION

According to Hueper (1942) cancer of the lung, under the name of "mala metallorum", was reported by Paracelsus in 1531 as occurring among miners in Schneeberg.

The disease was recognised by Baillie in 1796 (Morbid Anatomy).

Laënnec described cancer of the lung in 1805 in the Dictionnaire des Science Medicales, and again in 1819, in his famous treatise De L'Auscultation Médiate.

In 1837 Stokes in his Treatise on the Diagnosis and Treatment of Diseases of the Chest directed attention to the clinical manifestations, and in 1838 Carswell in his Pathological Anatomy emphasized the primary nature of the tumour.

During the latter half of the 19th Century many individual cases were reported. In 1897 West reported 155 cases from St. Bartholomew's Hospital and the Transactions of the Pathological Society.

In 1912 Adler in his monograph Primary Malignant Growths of the Lungs and Bronchi described 374 collected cases of primary lung cancer.

Bronchoscopic biopsy came into use between 1910 and 1915. Packard in 1917 described the clinical manifestations in terms of physical signs, X-Ray shadows and bronchoscopic findings.

Rosenblatt and Lisa (1956) describe necropsy studies since 1852. As far back as the period 1898-1902 Junghanns found primary lung cancer to account for 11.62% of all cancers seen at necropsy in Dresden.

Surgical resection for lung cancer had been attempted in 1916 by Morriston Davies, and in 1917 by Sauerbruch, but the first successful pneumonectomy for this disease was performed by Graham in America in 1933. In the same year two stage pneumonectomy was carried out by Price Thomas and Tudor Edwards. It was not until 1939 that the technique of dissection resection as we know it today was evolved, (Wooler 1957). Statistical trends will be discussed later, but in 1925 in England and Wales less than 3,000 deaths were recorded for respiratory cancer (larynx, trachea, lung and pleura, unspecified as to whether primary or secondary, male and female). By 1933 the figure was nearing 4,000 and it was approaching the 10,000 mark in 1946-7 after the end of the war.

As a result of these figures the Medical Research Council, in co-operation with other bodies, instituted studies into various aspects of the disease such as changes in the clinical approach to the disease. They also instituted research into cancer registration, carcinogens, smoking, and atmospheric

pollution, with workers such as Kennaway (1924) and Stocks (1924) who were already engaged on these problems. The publication of international statistics was undertaken by W.H.O. (Pascua 1952,1955), and C.I.O.M.S. (Clemmeson 1953).

Epidemiological information must be made available for the scientist, surgeon, statistician or pathologist.

Some of this information such as smoking habits, occupation, place of residence, previous medical history and pathology is best studied among groups of proved cases.

But in order to study age/sex incidence, the frequency of the various histological types, diagnostic criteria, and the value of death certification, absolute figures of operability, survival period and the average condition of the patients on first diagnosis it is necessary to include all the cases occurring in one area.

CHAPTER 2

ORIGIN OF THE CASES USED

This survey was planned to include every case of bronchial carcinoma occurring in the Blackburn Hospital Management Committee area during 1955.

A restrospective study based on death returns had been tried in previous years but it was found impossible to get adequate details and confirmation of findings. There being no cancer registration scheme in this area, it was decided to aim at recording and following up every new case first diagnosed during the year 1955. No cases under treatment or investigation from the previous year were included although of necessity some cases under observation during the preceding year were included if the diagnosis of lung cancer arose for the first time during 1955. From the 1st. of January 1956 no further new cases were studied but all the cases still under observation were continued to be studied, and were included in the series if the diagnosis was substantiated. The total number of cases is almost the same as the deaths reported for the area for 1955 by the Registrar-General, as will be seen from Table 1.

MUNICIPALITY	TYPE	POP.	M.	F.	CASES OF BR. CA. IN THIS SERIES DIAGNOSED IN 1955		REG.-GEN. DEATHS 1955	
		1951			M	F	M	F
BLACKBURN	C.B.	111217	51462	59755	48	10	47	7
ACCRINGTON	M.B.	40671	19270	21401	19	2	17	-
DARWEN	M.B.	30827	14399	16428	13	4	11	4
HASLINGDEN	M.B.	14505	6782	7723	1	-	4	2
B'BURN RURAL	R.D.	13245	6486	6759	3	-	5	-
OSWALDTWISTLE	U.D.	12133	5692	6441	2	2	3	3
CLITHEROE	M.B.	12057	5652	6405	5	1	5	1
GT. HARWOOD	U.D.	10738	4987	5751	4	-	6	-
CLITHEROE R.	R.D.	8661	4460	4201	-	-	-	1
CLAYTON LE MOORS	U.D.	6823	3233	3590	-	-	1	-
RISHTON	U.D.	5794	2757	3037	2	1	2	2
CHURCH	U.D.	5199	2451	2748	1	-	-	2
SURROUNDING OTHER RURAL AREAS (BRINSCALL, HELMSHORE, WEST BRADFORD, PADIHAM, ROSSENDALE)					4	1	2	1
		271870	127631	144239	102	21	103	23
					123		126	

TABLE 1. Comparison between morbidity (cases first diagnosed in 1955 and used in this series) and mortality for 1955 (deaths in the same area notified to the Registrar-General).

The Blackburn and District H.M.C. consists of a population of 271,870 made up of one County Borough, three Municipal Boroughs, five Urban Districts and two Rural Districts. The population of these areas, male and female is shown in Table 1.

This area is served by one General Hospital, the Blackburn Royal Infirmary, of 400 beds; one larger hospital, also in Blackburn, taking more chronic cases, called Queens Park Hospital. The largest of the Municipal Boroughs has a small General Hospital called Accrington Victoria Hospital. This and the Blackburn Royal Infirmary have out-patient Departments and there are also two chest clinics, one in Accrington and one in Blackburn and two small sanatoria, one attached to the Fever Hospital called Park Lee and one called Withnell Hospital.

During 1955 each of these hospitals and clinics was visited once or twice a week, and with the co-operation of the various X-Ray Departments a note was made of every X-Ray report that suggested the possibility of a bronchial carcinoma. With the permission of the various consultants, a further check was kept by all the medical clerks in the group, so that I would not miss any case, and if possible I could visit the patient. Some advanced cases were only referred to the hospital once for an X-Ray and subsequently treated at home after a domiciliary visit by a consultant. The consultants very kindly drew my attention to any such cases. A few were treated at home and never referred to hospital at all. One or two others moved into the area after investigations or treatment had been done elsewhere. Some of these cases I learned

about through the Chest Clinics, other cases I found out from the weekly death sheets and had to obtain the details retrospectively. The weekly death returns from all the districts shown in Table 1 were studied each week and for the first six months of 1956. All operation notes, necropsy, bronchoscopy findings etc. were extracted from the original records.

In this manner during 1955 I collected case notes and made diagrams of the X-Ray pictures of 254 cases in which a diagnosis of bronchial carcinoma had been made or was a possibility. Some of these were quickly diagnosed and treated as bronchial carcinomas, while others remained under observation for varying periods. By the end of 1955 however about 120 cases of bronchial carcinoma had been diagnosed. During the next year one or two were added from the observation or rejected cases and one or two were taken off the list as not confirmed. For the most part the work during 1956 consisted of entering into my notes all developments regarding the patients, operation findings, out patient attendances, fitness for work, re-admissions to hospitals, and if ~~half~~ they died, a copy of the certified cause of death and post-mortem report, if any.

Table 2 shows to which hospital department these 254 cases were initially referred.

FIRST REFERRED TO:-	BRONCHIAL CARCINOMAS	UNCONFIRMED CASES THOUGHT AT FIRST MIGHT BE BRONCHIAL CARCINOMAS
PRIVATE	2	
CHEST CLINIC	20 (4 M.M.R.)	48 (1 M.M.R.)
HOSPITAL OUT-PATIENTS	50	44
M.O.P.D.	41	39
S.O.P.D.	7	2
E.N.T.	1	1
REFERRED FROM MENTAL OR OTHER INSTITUTION	1	2
HOSPITAL IN-PATIENTS	48	39
MEDICAL	39	35
SURGICAL	5	3
E.N.T.	3	0
TRANSFER FROM MENTAL OR OTHER INSTITUTION	1	1
G.P. ONLY & DOM. VISIT (NO X-RAY)	3	
	123	131

TABLE 2. First referral of 123 cases of bronchial carcinoma and 131 cases of suspected bronchial carcinoma.

Only one sixth of the cases were referred in the first instance to the Chest Clinics. A few of these cases, about 5% of the total, were then investigated in sanatoria.

The remaining five sixths were equally divided between the hospital out-patient and in-patient departments with or without a preliminary domiciliary visit.

Cases relapsing were readmitted to General Hospitals or Sanatoria in the ratio of about 3 : 1.

As a check of the numbers obtained I wrote to the Registrar General at the end of 1956 for the 1955 death figures for this area. These are shown in Table 1 for each municipal area. I had collected 123 live or recently dead cases during the year against 126 recorded deaths.

As a second check on my figures I compared my incidence with the death rate for males and females for England and Wales as a whole for 1955. The Registrar General's Quarterly Return for the 1st. Quarter of 1956 gives the death rate from malignant neoplasms of lungs and bronchus for 1955 as 39 per 100,000 for the total population; 70 per 100,000 for males and 12 per 100,000 for females.

My incidence figures were 45 per 100,000 for the total local population; 81 per 100,000 for males, and 14 per 100,000 for the females. These figures are very nearly equal to the local death rate figures for Blackburn given (ibid) (for both sexes combined) as 50 per 100,000. A number of industrial or metropolitan areas give a much higher figure, e.g. Shoreditch (79 per 100,000), while some other non-industrial towns give a

much lower figure e.g. Scarborough (34 per 100,000).

CHAPTER 3

DIFFERENTIAL DIAGNOSIS

Chapters three and four illustrate the difficulties of diagnosis, and the cases are dealt with in detail to try to assess the degree of accuracy of diagnosis finally obtained.

Table 3 shows the differential diagnosis of the total 254 cases studied. Malignancy was confirmed in approximately 50%

It is now proposed to discuss briefly the differential diagnosis of the 131 cases in which the presence of a carcinoma was not confirmed. These have been called C $\overline{111}$ cases in this series.

A. PNEUMONIA AND POST-PNEUMONIC FIBROSIS

The most common condition was pneumonia and post-pneumonic fibrosis. Such inflammatory changes simulating carcinoma, occurred in 31 cases (28 male, 3 female), and 16 of these required bronchoscopy.

Two cases required thoracotomy to establish the diagnosis. The first of these, Figs, 1a and b, (Harwood - 140), was a man aged 48, with a short history of two months pain, fever and staining, rales over the right lower lobe, and a brassy cough. Bronchoscopy was negative. The shadowing was unchanged after 10 weeks so, although our impression was that it was inflammatory, thoracotomy was advised. This showed a mass involving the right middle and lower lobes with glands around the right main bronchus and trachea. Pneumonectomy and radical

DIAGNOSIS	MALE	FEMALE	TOTAL
BRONCHIAL CARCINOMA	102	21	123
PNEUMONIC AND POST-PNEUMONIC FIBROSIS	28	3	31
PULM TB ACTIVE OR INACTIVE	20	6	26
BRONCHIECTASIS	15	1	16
SECONDARY NEOPLASMS	9	3	12
CARDIAC CONDITIONS	9	3	12
CHRONIC BRONCHITIS AND EMPHYSEMA	10	-	10
BRONCHIAL CARCINOMAS DIAGNOSED IN 1953-4-6-7	10	-	10
CYSTIC DISEASE	1	-	1
ALSCESS OF LUNG	2	-	2
EMPYEMA	2	-	2
ONE EACH RETRO-STERNAL THYROID, BRONCHIAL TELANGIECTASIS		2	2
ONE EACH HYSTERIA, EPILEPSY, CARCINOMA OF TRACHEA, MEDIASTINAL CYST, PHACYNGEAL PUNCH, LYMPHATIC LENKAEMIA, FOREIGN BODY.	7		7
	113	18	131
	215	39	254

TABLE 3. Differential diagnosis of 254 cases occurring in Blackburn in 1955 all of whom it was thought at one time might be bronchial carcinomas.

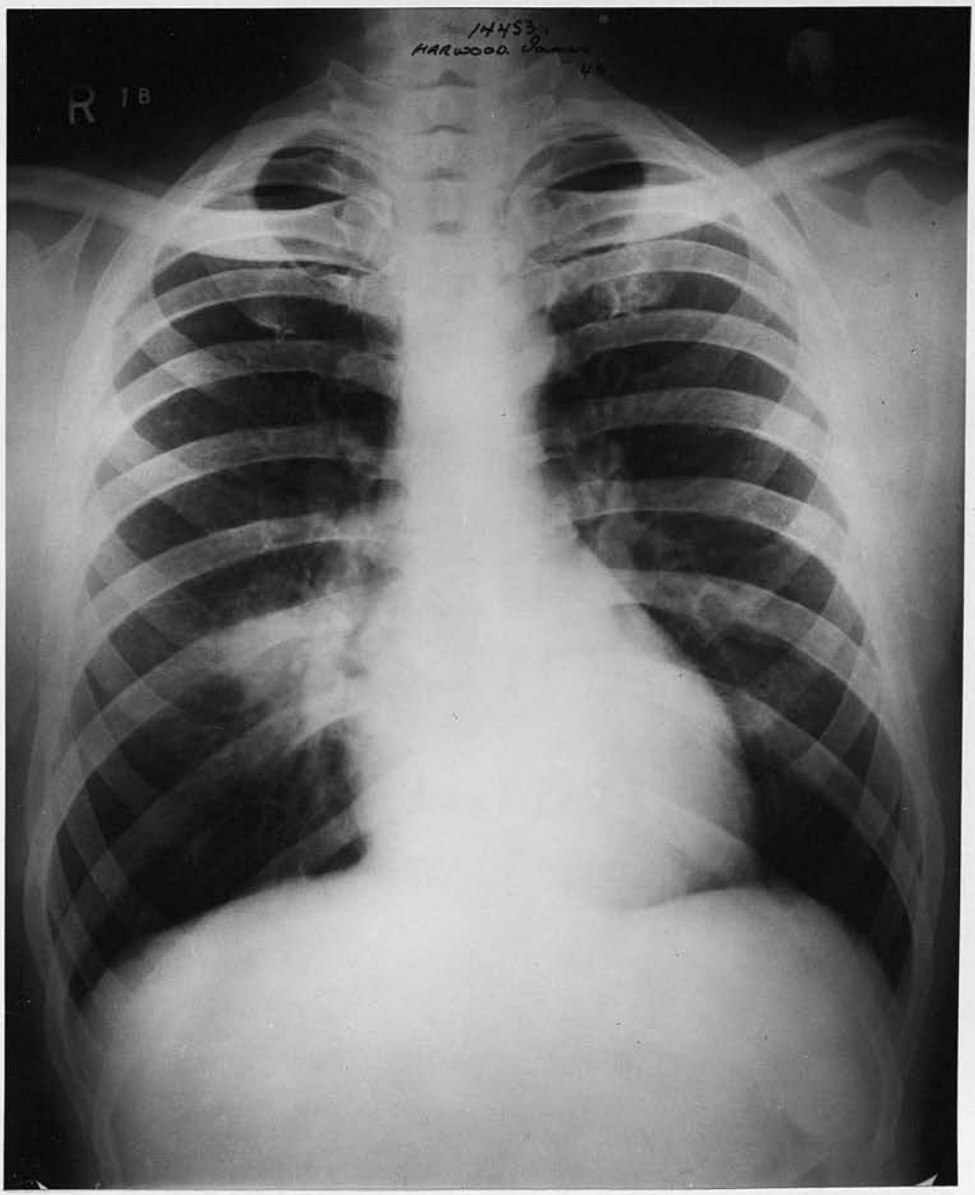

FIG. 1a. - Non-specific pneumonitis simulating bronchial carcinoma.
Male, age 48, 2·9·55. (Harwood-140).

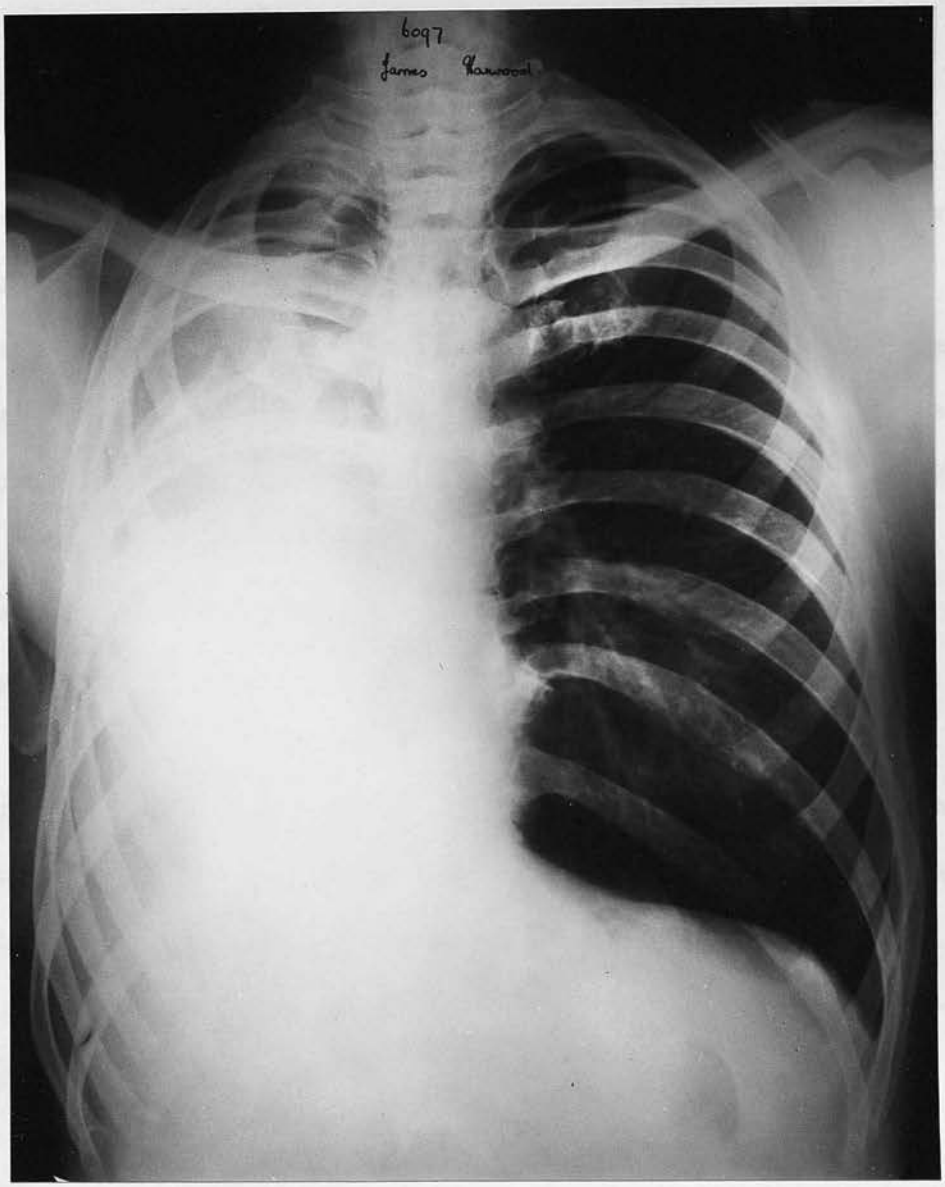

FIG. 1b. - Do. After pneumonectory.

gland clearance was carried out, but histology did not show a carcinoma. There had however been extensive destruction of tissue due to septic pneumonitis. The patient made a complete recovery.

The second inflammatory case requiring thoracotomy was a coal miner aged 57. (Thompson - 273).

He had smoked 25 cigarettes a day for 40 years and had had pneumonia 14 years before. He had had increasing attacks of chronic bronchitis for the last five years with much putrid purulent sputum, gross clubbing, shortness of breath and some slight loss of weight. A few weeks before he had noticed a trace of blood in the sputum. His X-Ray is shown in Fig. 2.

At bronchoscopy an obstruction in the right lower lobe bronchus was seen with much pus oozing out. Biopsy showed a simple infective granuloma.

Right middle and lower lobectomy revealed a mass of fibrous tissue, in the centre of which was a piece of beef bone. When told of this the patient remembered inhaling such a piece of bone about ten years before.

One case, with a simple inflammatory lesion, (Bradley - 218), required two periods of hospital treatment and three bronchoscopies over a period of thirteen months to exclude carcinoma.

No doubt, in the past some carcinomas were diagnosed as pneumonias, particularly among the older age groups. Such cases nowadays may be kept alive with antibiotics long enough to reveal the true diagnosis. Yet in only 2 cases in this series did shadowing, due to or associated with, a carcinoma

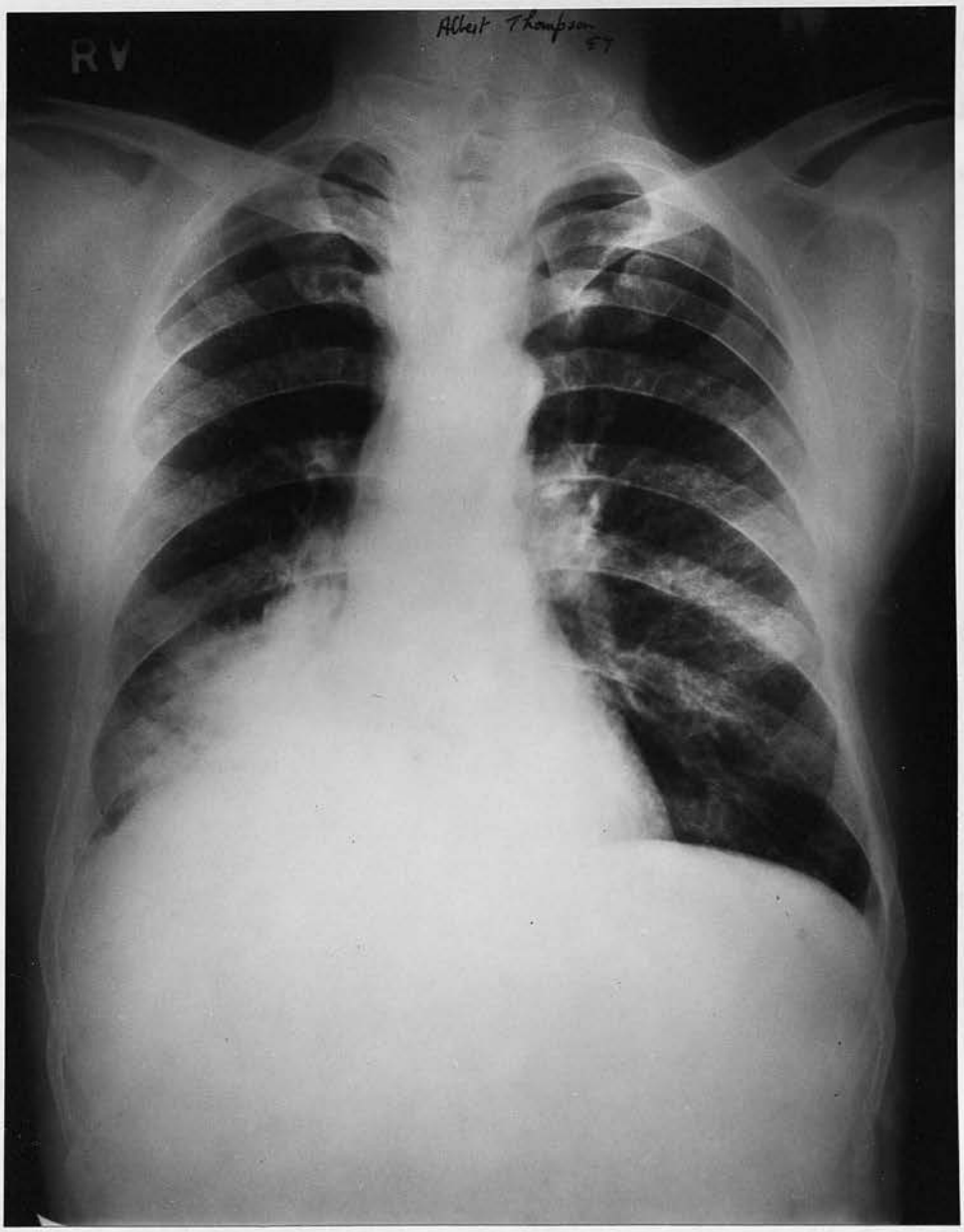

FIG. 2. - Inflammatory reaction to foreign body simulating carcinoma. Male, age 57, (Thompson - 273-).

regress with chemotherapy and that only to a slight degree. On the other hand thirteen cases of severe but true pneumonia might have been diagnosed as bronchial carcinomas had they not recovered with intensive chemotherapy.

For instance one case of severe staphylococcal suppurative pneumonia in a man aged 65 years took over 12 months to clear even with modern antibiotics, (Jenkinson - 47). He had been off work for 6 months, with severe dyspnoea, clubbing of the fingers and loss of weight of two stones. The X-Ray report stated: "more suggestive of a bronchial carcinoma than an inflammatory lesion". The elective diagnosis at the height of the illness was definitely bronchial carcinoma, and the physician told me that had the patient died then, in the absence of a post-mortem the case would have gone on the death certificate as a bronchial carcinoma.

Of the 13 cases mentioned 6 had a short history of 2 weeks or less, but only in 7 cases did the X-Ray picture quickly clear. The average age was 57 years, and four cases had fluid.

One of these 13 cases, (Standen - 81), illustrates the difficulty of diagnosing a pneumonia plus effusion in an elderly man. This patient aged 52, had had bronchitis for 5 months, with breathlessness and pain for one month, pyrexia and specks of blood. The fluid was straw-coloured and negative for T.B. and malignant cells. His liver was thought to be enlarged. Bronchoscopy was negative but inoperable carcinoma was suspected. Slowly however, over about 10 months the whole thing cleared up. It is very difficult to

exclude a tuberculous element in some of these effusions in elderly men. Again cases have been described where a small basal effusion with an otherwise clear X-Ray was found to be due to carcinoma in the terminal bronchioles.

It is interesting to note the sex ratio of 5 : 1 among the pneumonic and post-pneumonic group.

Of the inflammatory group two remain under serial observation and there is a slight chance that they may yet prove to be carcinomas. They are both working.

One of them (Hargreaves - 63) is a man aged 63 with a long history of chest trouble and some pneumonitis-like shadowing in the left upper lobe. He still occasionally suffers from blood stained sputum but he refuses investigation.

The other case (Elliott - 97) is a young man of 37 who also refuses investigation. He has a chronic abscess-like shadow in the right lower lobe.

B. TUBERCULOSIS

The tuberculosis group of the 131 non-carcinoma patients, though less numerous than the inflammatory group described above, was even more difficult to differentiate, especially with regard to cavities, coin shadows, and hilar masses. The lesions in tubercle as in carcinoma rarely present as pure lobar shadows which quickly clear.

In this group there were 20 males and 6 females. Twenty required hospital investigation and eight required bronchoscopy to settle the diagnosis.

Two cases were initially diagnosed as bronchial carcinomas and subjected to lobectomy.

One of these, (Caddy - 269), was a man aged 53 with a dense left upper lobe lesion. The history of six months cough and occasional blood stained sputum and shortness of breath was quite typical of carcinoma. Left upper lobectomy was carried out and some enlarged mediastinal glands were removed without tuberculosis being diagnosed. Histology however revealed gross tubercle with cavity formation and there was evidence of tubercle in the mediastinal glands.

The second thoracotomy case, (Riding - 132), was a man aged 62 who had a right upper lobectomy for a small solitary cavity. His only symptom had been haemoptysis. Laryngeal swabs were negative to culture and his sputum had also been negative when tested for malignant cells.

A third case (Diggles 163), was advised thoracotomy but refused. He was a man aged 55 years with a left apical cavity. He agreed to chemotherapy at home and, after 3 months streptomycin, tomograms showed simply a very fine thin-walled cyst.

We have one case still alive who is probably tubercle but in whom a diagnosis of carcinoma has not yet been completly ruled out.

He is a man aged 60, (Birchall - 69), with a long history of bronchitis and pneumonia who has been staining for over three years on and off. His X-Rays show what appears to be a small area of pneumonitis in the first right interspace

which has got very slightly bigger over three and a half years. He carries on working and although he is thought to have old tuberculous scarring he may well prove to be a carcinoma. He has been twice rejected for thoracotomy on account of breathlessness.

There are two cases, now dead, in which it was not possible to decide between tubercle and bronchial carcinoma.

The first case was an engineer, (Aspden - 28), aged 59; an active man who had fractured an arm in an industrial accident in 1939. He gave a history of pneumonia in 1924 and cough and very occasional staining for 1 year. He had twice been in bed with bronchitis. He had chubbing and his B.P. was 180/90. He was admitted to hospital in May 1955 and his chest X-Ray showed some minimal mottling above the right cupola. Bronchoscopy was negative and his chest X-Ray cleared. Heart and E.C.G. were normal. He returned to work but was still staining slightly on occasions. His chest X-Ray was repeated on 5-9-55 and this was clear. Two weeks after he had a fatal haemoptysis and died. In view of his industrial injury the coroner ordered a post mortem which was alleged to show tuberculosis disease and cavitation in the right lower lobe. In the absence of histology we thought carcinoma a possibility.

The second case was an old man of 77, (Lyons - 238), who had been well until four months before, when he had been admitted to a geriatric ward with cough and emphysema heart failure, cyanosis, diarrhea, pyrexia and incontinence. He had a severe anaemia but sternal puncture was normal. On two occasions his sputum showed cells of epithelioid type showing

mitosis, and the geriatrician suspected bronchial carcinoma. His chest X-Ray showed bilateral stippling with heavy roots.

When he died it was proposed to give the cause of death as "anaemia carcinomatosis, source unknown", but as the patient had been a bricklayer for 60 years the coroner ordered an inquest. A necropsy was done which showed macroscopic evidence of tuberculous broncho-pneumonia, and this was given as the cause of death. Histology did not however bear out the diagnosis of tuberculosis and we thought a diagnosis of emphysema heart failure might have been preferred.

There were also two cases, (Clarkson - 25, and Dillan - 52), in which a proved bronchial carcinoma was accompanied by active tuberculosis.

Not strictly coming within the non-carcinoma group described in this chapter are three cases originally diagnosed as tubercle that turned out to be bronchial carcinomas.

The first of these, (Pomfret 270), aged 61, was an M.M.R. pickings with minimal right apical calcification and a little heaviness at the right roof. Six months later he had developed some pain and a few spots of blood. He developed dysphagia and cervical nodes and was soon inoperable.

The second carcinoma that was initially diagnosed as tubercle is shown in Fig. 3 (Westwell - 54). He was aged 54 and had been a miner for a few years in his younger days. He had had some chest pain and bronchitis since 1938 and had been referred to the Chest Clinic in 1951 when his X-Ray was as shown in Fig 3a. Personally I don't know whether the left

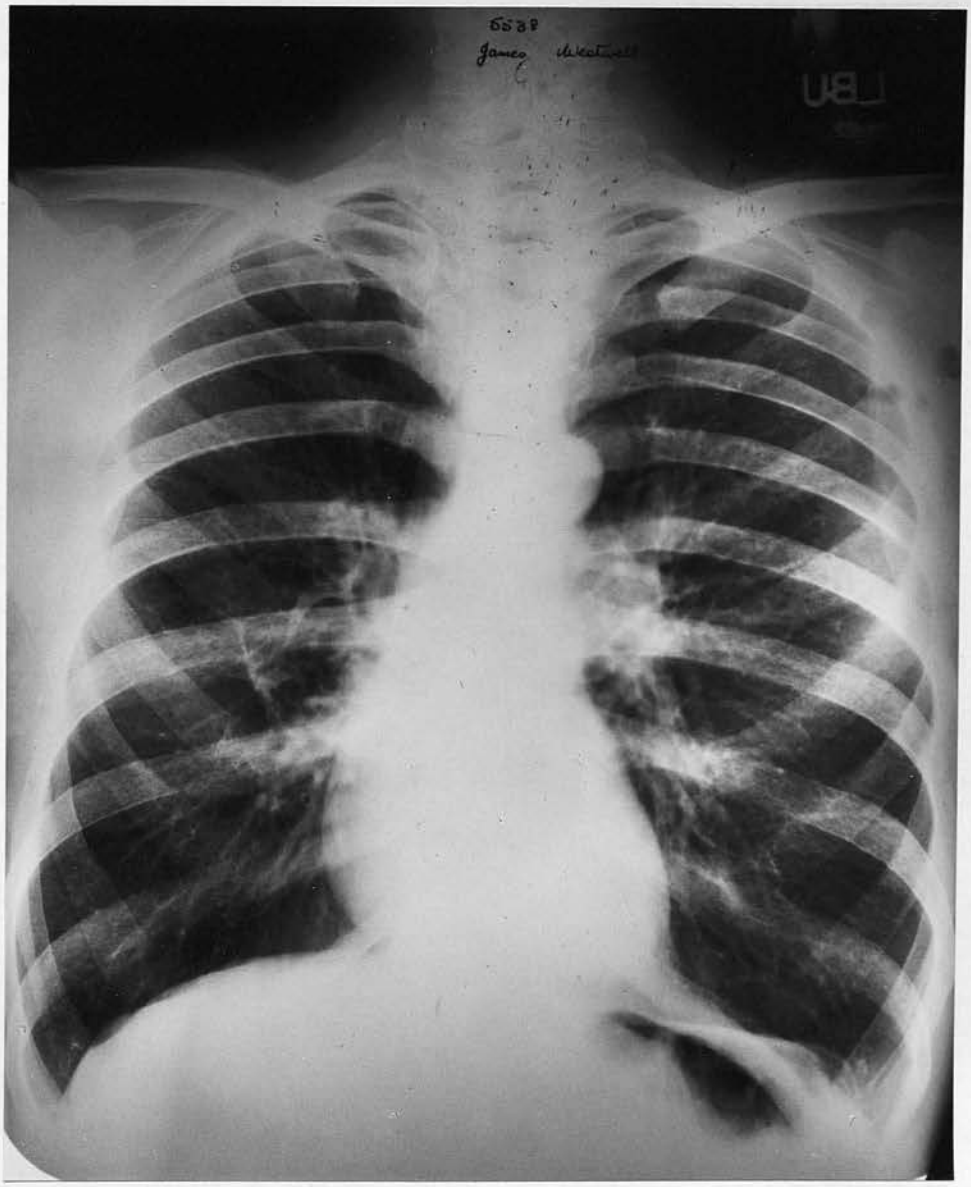

FIG. 3a. - Carcinoma with long history, simulating tuberculosis.
Male, age 54, 13·11·51.
(Westwell - 54).

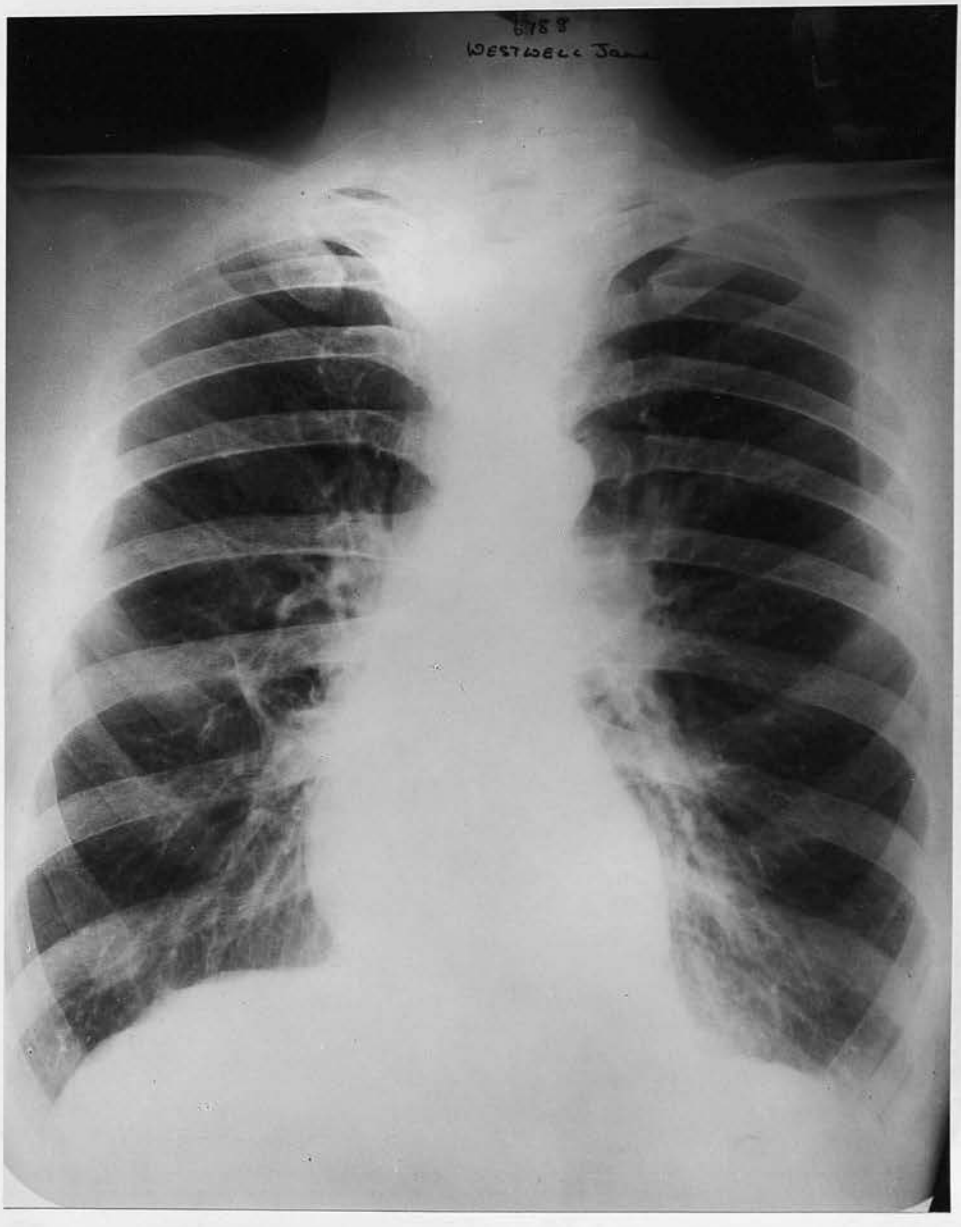

FIG. 3b. - Do. 26.xi.53.

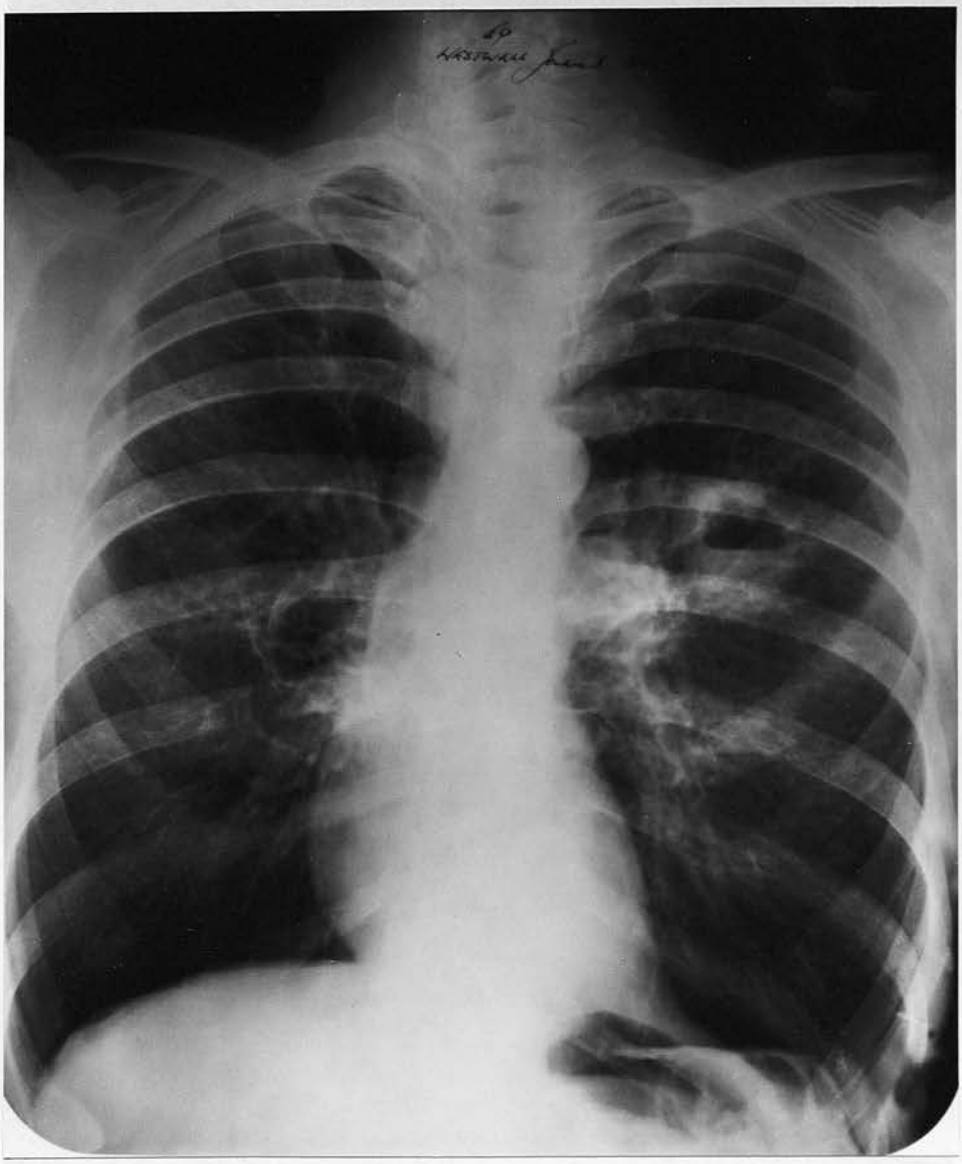

FIG. 3c. - Do. 4.3.55. Malignant cavity.

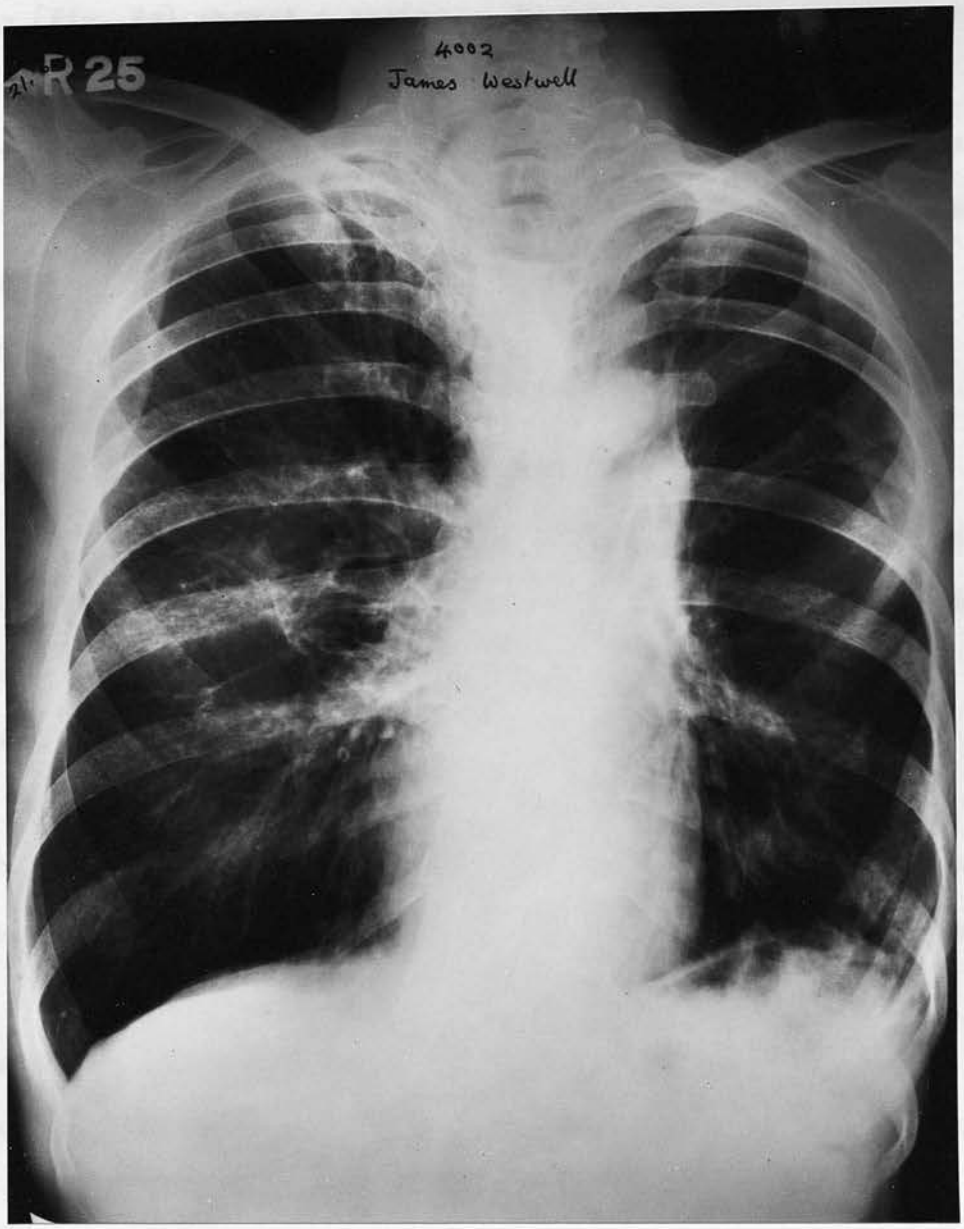

FIG. 3d. - Do. 16.2.56. After left upper lobectomy.

root was normal or not then. He was seen again once or twice for his bronchitis and Fig. 3b shows the condition two years later. In January 1955 he brought up some blood and his X-Ray (Fig. 3c) showed a cavity. Bronchoscopy was negative and he was notified as tubercle and admitted to a sanatorium. Two months later cancer cells were found in the sputum and a squamous cell carcinoma was removed. (Fig. 3d). Bronchoscopy just before the operation was still negative. The mediastinal and paratracheal glands were involved which was not surprising. His symptoms of pain went back 17 years. However he is still alive but not well or working.

The third case, (Van Hussell - 271), a man aged 58, was referred by his doctor because of offensive sputum and slight haemoptysis after flu. His chest X-Ray (Fig. 4a) appeared normal.

Twenty-two months later he was referred by Mass Radiography, (Fig. 4b), with some vague shadowing in the right upper lobe and an occassional ache in that region. He still had a cough.

An X-Ray taken one month later (Fig. 4c) now showed a cavity in the second right interspace, as well as a few calcified nodes at the left root and at the periphery of the 2nd. left interspace.

The condition was thought to be tubercle. He gained weight and seemed better with treatment. Sputums were negative but he was wheezy and somewhat short of breath.

After another 12 months he was still well and working but his chest X-Ray (Fig. 4d) showed collapse of the right upper lobe, which was due in fact to a carcinoma which had been

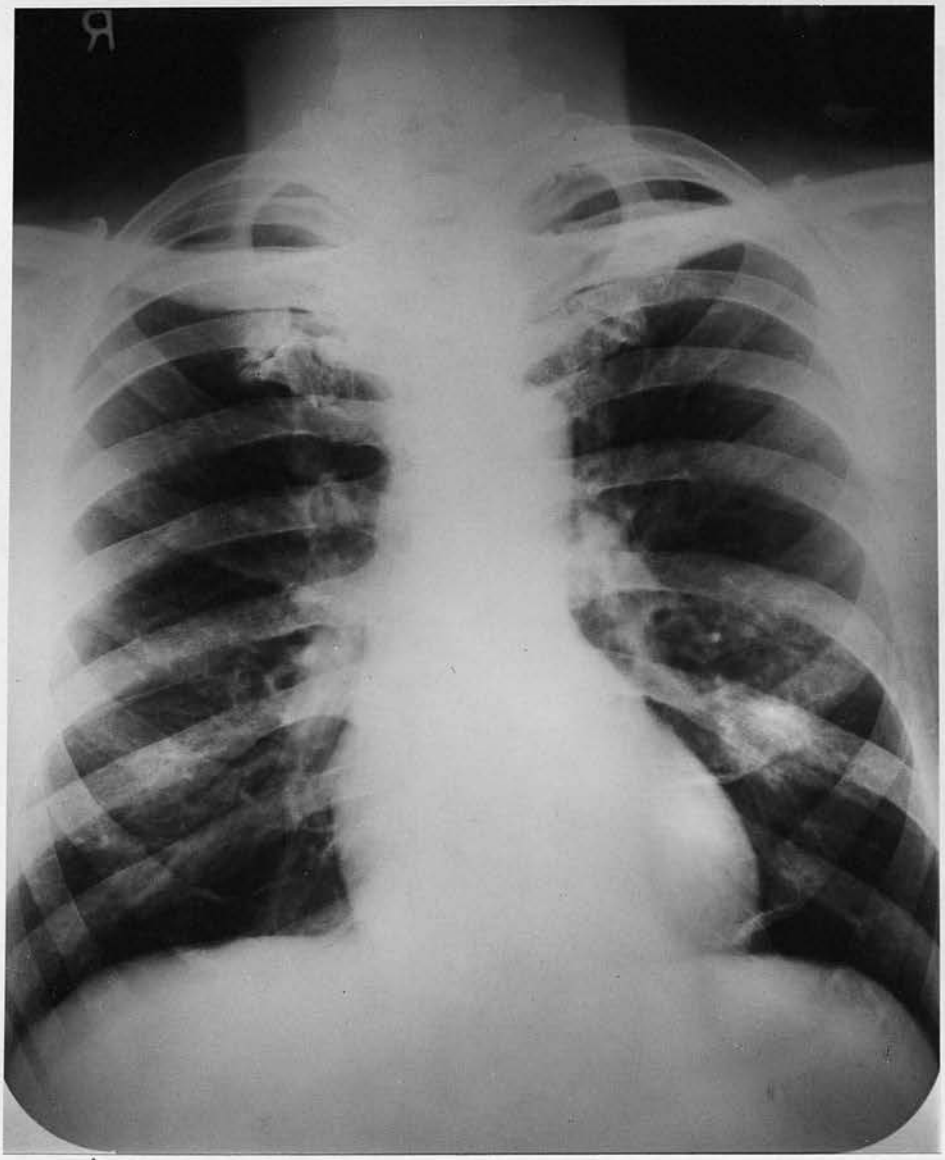

FIG. 4a. - Carcinoma simulating tubercle.
Clear film but patient has had
haemoptysis. Male, age 58, 23.4.52.
(Van Hussell-271).

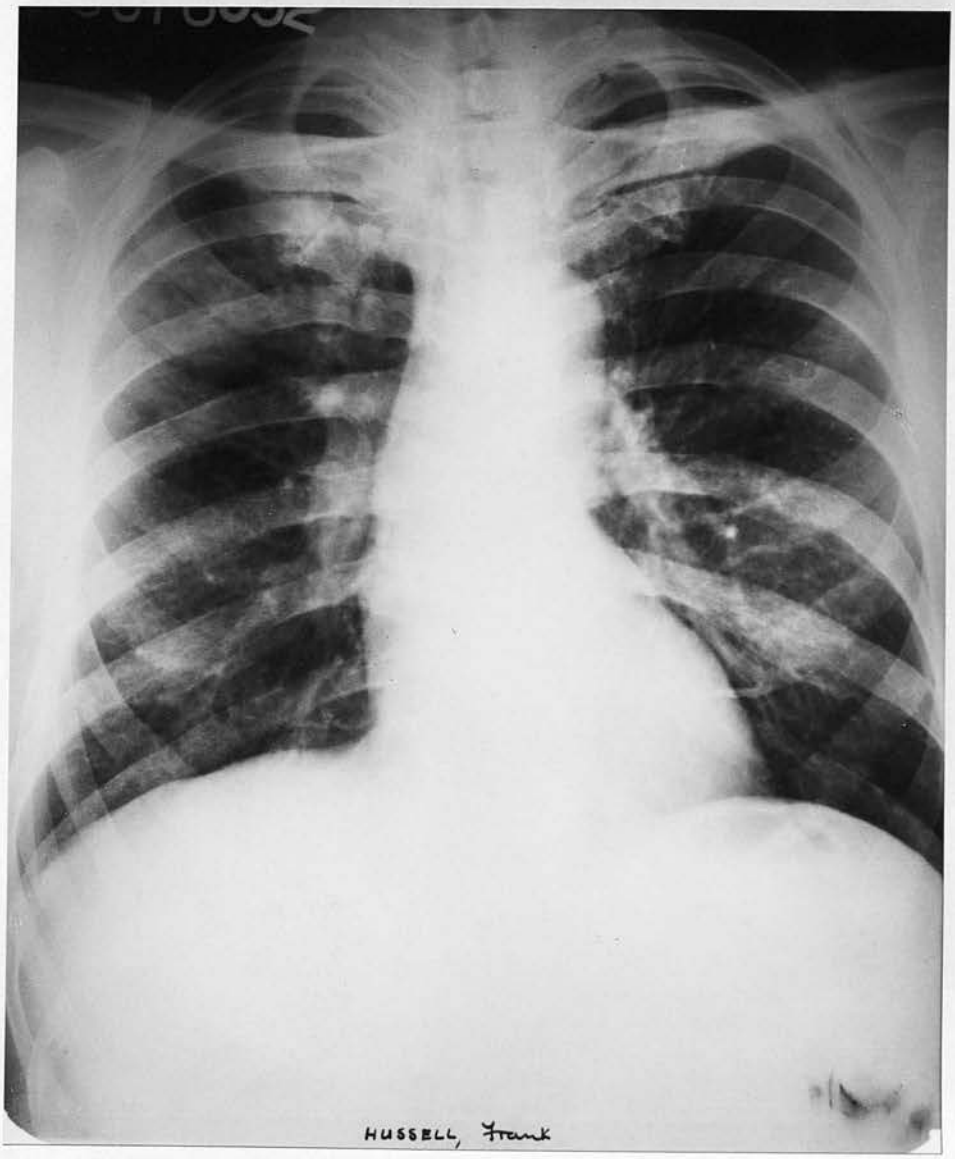

FIG. 4b. - Do. 27·2·54.

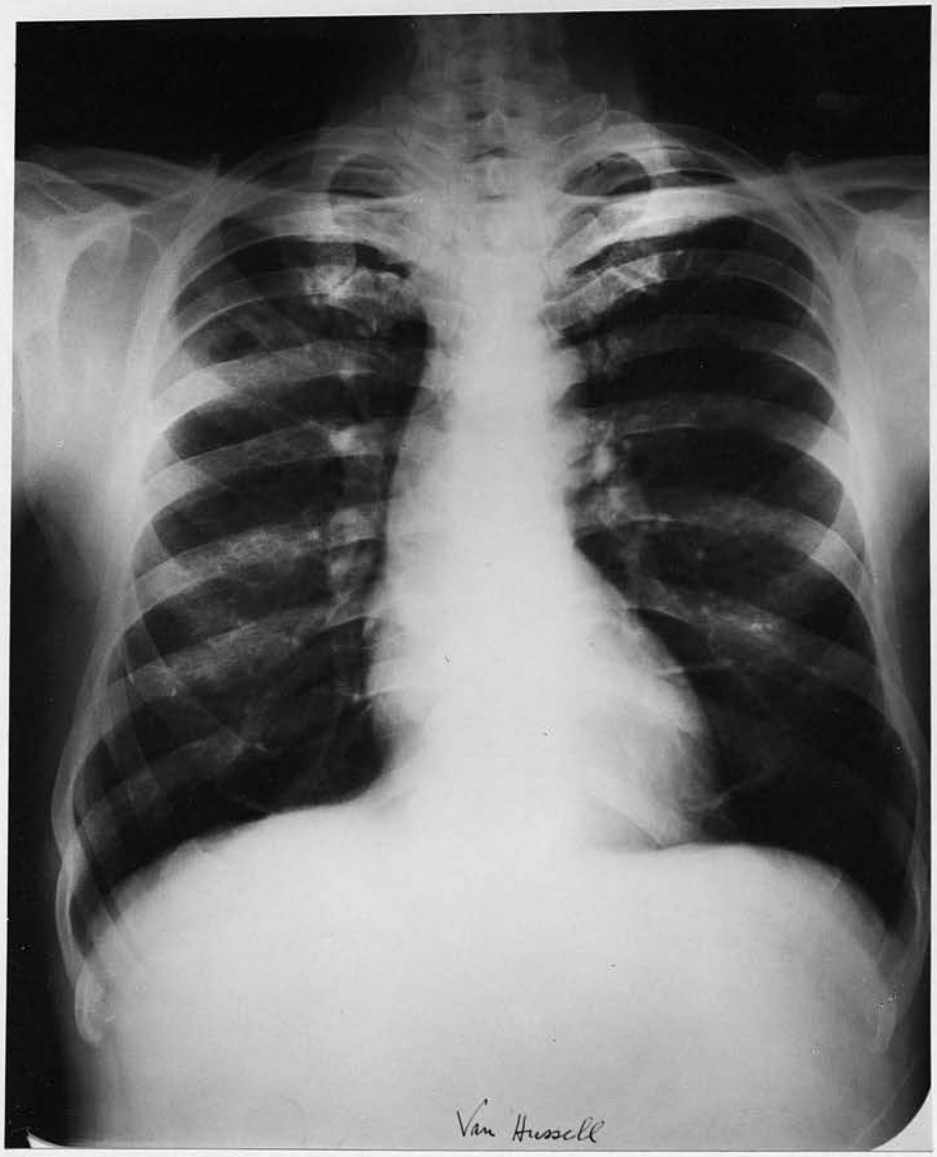

FIG. 4c. - Do. 16·3·54.

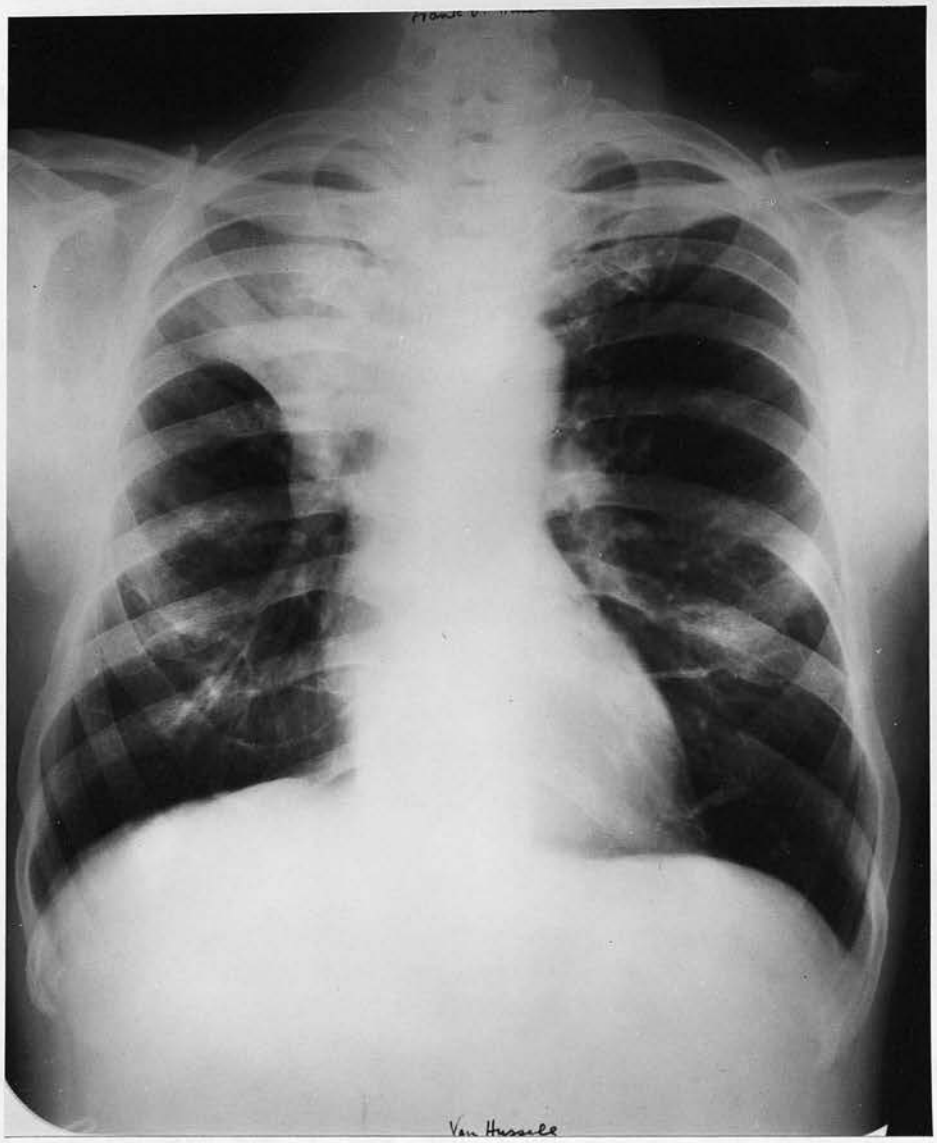

FIG. 4d. - Do. 13·7·55.

growing under serial X-Rays for three years. He was given deep X-Ray therapy but died after another year. The whole course of the disease apparently occupied some four to five years.

The following list shows the difficulty experienced in excluding 26 cases of tubercle from 254 cases of suspected carcinoma.

20 cases required hospital investigation.

8 required bronchoscopy.

2 required thoracotomy.

1 was advised thoracotomy but refused.

1 case still alive unseparated.

2 cases now dead unseparated.

2 cases of bronchial carcinoma plus tubercle.

3 cases of bronchial carcinoma indistinguishable for several months ~~for~~ from tubercle.

C. BRONCHIECTASIS

Sixteen cases of bronchiectasis (15 male, 1 female) occurred among the non-carcinoma cases.

This may seem a relatively large number in view of the average age, 54 years. Eleven of the cases however presented with haemoptysis and it was this that raised the question of carcinoma. Of the 16 cases 8 required bronchoscopy.

D. SECONDARY NEOPLASMS

Twelve cases of secondary neoplasms in the lungs were followed up, as primary lung cancer could not easily be ruled out. When they died the certified causes of death were given as follows:-

3 cases carcinoma stomach

2 cases carcinoma breast

2 cases cerebral tumour

1 case carcinoma oesophagus

1 case carcinoma tongue

1 case carcinoma pancreas

1 case carcinoma cheek

1 case general carcinomatosis,
source unknown.

In no case was pathological or histological proof obtained, although the two breast cases had previously been operated on. Likewise the cases of tongue and cheek had previously been diagnosed as such.

Four of the cases, however, we thought could equally well have been diagnosed as primary bronchial carcinomas.

The first of these four cases, (Plummer-108), was a man aged 51 years admitted to hospital with signs of a brain tumour, confirmed by carotid arteriogram. Biopsy through a burr hole had suggested either a glioblastoma or a metastatic oat-celled carcinoma of bronchial origin. Unfortunately no necropsy was carried out the cause of death being given simply as "malignant tumour right cerebral hemisphere".

The second case was a man of 62, (Ashworth - 24), who had had bronchitis for 20 years. He had been off work for 10 years and for six months had had increased coughs and sputum, haemoptysis once, a hoarse voice and variable dysphagia. He

was dyspnoeic and cachectic. His chest X-Ray showed some indefinite shadows outside the left lower heart border. He had a firm lump half an inch in diameter in the left lumbar region considered to be a secondary. He also had an enlarged hard gland half-way down the posterior border of the left sterno-mastoid. There was no prospect of treatment in this case and when he died at home he was written up as a carcinoma of the oesophagus.

The third case, a man aged 54, (Lassie - 35), had had a cough since having an operation for duodenal ulcer in 1928. He was admitted to hospital in February 1955 with abdominal pain, vomiting, tenderness over the liver and a secondary nodule in the abdominal wall. Biopsy suggested secondary carcinoma of bronchial origin. His chest X-Ray showed a small left pleural effusion.

He went rapidly down-hill on discharge from hospital but the abdominal symptoms predominated and the certified cause of death three months later was carcinoma of the stomach. No necropsy was performed.

The fourth case (Tattersall - 16) was a man aged 77 with vague shadowing along the left lower heart border, haemoptysis, and pains in the chest for three months. We were content with a diagnosis of bronchial carcinoma but terminally abdominal symptoms predominated and the cause of death was given as cancer of the stomach on clinical grounds.

A fifth case, in this group, still alive may yet prove to be a bronchial carcinoma, (Roebuck - 149). His symptoms were

neurological from the start with agraphia, left hemiplegia and slurred speech. His chest X-Ray was clear except for a definite paralysis of the left cupola.

E. CARDIAC CONDITIONS

Twelve cases with suspicious shadows were eventually diagnosed as cardiac. Five of these had had haemoptysis. All except one gave a definite and continuous history of one year or more, and in every case the heart was enlarged on X-Ray.

The average age was 63 and there were three males and nine females. One case required bronchoscopy.

There were two cases of pulmonary infarction, both of which and one other case showed shadowing outside the left lower heart border. Four cases showed an exaggerated shadow of the right root. In three cases an effusion was present.

One case, (Smith - 182), shows the difficulty of diagnosis in the elderly. He was a man aged 72 who had had bronchitis for years. He was feeling quite well until one day before being admitted to hospital with severe pain in the right chest, dyspnoea, orthopnoea, tachycardia 130, with irregularity, and blood stained sputum. His chest X-Ray, Fig. 5a, showed pulmonary congestion, and right basal shadowing. A diagnosis of pneumonia with heart failure was made, but, as he died the day after admission, a post mortem was considered necessary. This revealed a bronchial carcinoma and a purulent pericarditis with effusion. The pericarditis can, I think, be made out in the lateral X-Ray film (Fig. 5b).

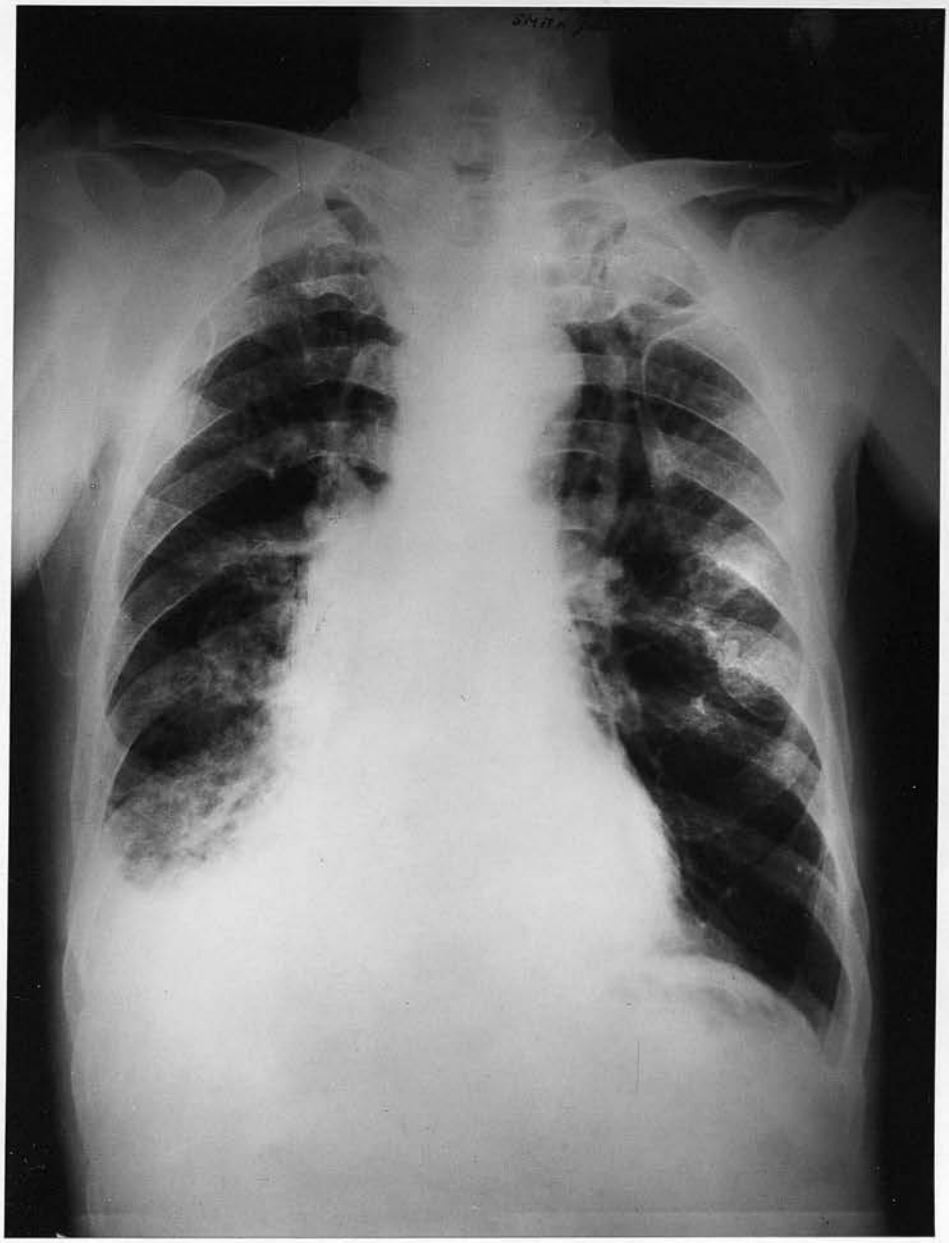

FIG. 5a. - Bronchial carcinoma with history of 1 day. Male, age 72, 2.9.55. (Smith - 182).

FIG. 5b. - Do. Showing purulent pericarditis,
13.9.55. (Five days before death).

Whether any of the twelve cardiac cases described in this section were indeed carcinomas I don't know. One case with a hemiplegia still under observation (Eddleston 227) may yet prove to have a carcinoma.

F. CHRONIC BRONCHITIS AND EMPHYSEMA

The 10 cases of chronic bronchitis and emphysema naturally gave a longer history even than the cardiac cases, the minimum period being 2 years. The average age was 57 and all the patients were males. In 8 cases the X-Ray query concerned possible root enlargement. Often a root may appear abnormally heavy. Very occasionally after being watched for two or three years it becomes the site of a carcinoma. Haemoptysis was present in three cases and pains in two. Only one case was bronchoscoped.

Two of these remain under observation, (Watson 185, Heywood 220).

A review therefore of 131 cases in which the clinicians, after being suspicious of bronchial carcinoma, rejected this diagnosis, leaves a doubt in 13 cases or 10%. This is made up as follows:-

2 cases, still alive, diagnosed as inflammatory that may possibly be bronchial carcinomas.

1 case, still alive, diagnosed as tuberculosis that may well be a bronchial carcinoma.

2 cases, now dead, that were diagnosed as tuberculosis and may have been bronchial carcinomas.

1 case, now dead, diagnosed as a cerebral tumour that may have been a bronchial carcinoma.

1 case, now dead, diagnosed as carcinoma of the oesophagus, that may have been a bronchial carcinoma.

2 cases, now dead, diagnosed as stomach carcinomas that may have been bronchial carcinomas.

1 case, still alive, withhemiplegia of unknown origin that may possibly be a bronchial carcinoma.

1 case with a hemiplegia thought to be due to cerebral embolism that may possibly be a bronchial carcinoma.

2 cases of chronic bronchitis still alive, that may possibly be bronchial carcinomas.

CHAPTER 4

CLASSIFICATION OF BRONCHIAL CARCINOMA CASES ACCORDING TO CRITERIA OF DIAGNOSIS

The 123 cases accepted as bronchial carcinomas have been classified into three groups according to the degree of certainty of the diagnosis.

The cases confirmed histologically or pathologically have been designated CIA. There are 66 such cases, (57 male, 9 female), making 54%.

Cases in which the diagnosis is considered to be beyond doubt by virtue of the history, clinical findings and X-Rays (in the absence of histological/pathological evidence) have been designated CIB. There are 21 such cases (17 male and 4 female) or 17%.

The third group consists of the remaining 29%, i.e. 36 cases, (28 male and 8 female), in which the diagnosis, though very likely in about half the cases, is open to varying degrees of doubt. The cases in this group have been designated C II cases.

Table 4 sets out the average age, the duration of symptoms before diagnosis, and the survival period after diagnosis for these three groups. The figures given are averages and the duration of symptoms before diagnosis is at best an approximation.

Table 4 shows that the doubtful, (C 11), cases represent an older age group with a shorter duration of symptoms and a shorter survival period.

CRITERIA OF DIAGNOSIS	NO. OF CASES	AVERAGE AGE	DURATION OF SYMPTOMS BEFORE DIAGNOSIS (WEEKS) (APPROX).	SURVIVAL TIME AFTER DIAGNOSIS (WEEKS).
DIAGNOSIS CONFIRMED HISTO-PATHOLOGICALLY.				
FEMALE (FCIA)	9	58	45	(1 Alive) 26
MALE (MCIA)	57	57	34	(6 Alive) 21
DIAGNOSIS CLEAR				
FEMALE (FCIB)	4	62	40	13
MALE (MCIB)	17	63	28	(1 Alive) 13
DIAGNOSIS OPEN TO DOUBT				
FEMALE (FCII)	8	69	23	9.5
MALE (MCII)	28	67	25	(1 Alive) 14
ALL FEMALE CASES	21	63	36	(1 Alive) 16.7
ALL MALE CASES	102	61	31.5	(8 Alive) 18.7
ALL CASES	123	61	31	(9 Alive) 18.4

TABLE 4. - Age, duration of symptoms before diagnosis, and survival period after diagnosis, of the carcinoma cases according to criteria of diagnosis.

They were in fact mostly terminal neglected cases. Of the 36 cases, only seven had bronchoscopy examination. This was negative in five cases and indefinite in two.

A typical example of this "doubtful diagnosis" group is a man who was initially thought to be tubercle, but was finally certified as dying from a bronchial carcinoma. (Pearson-1).

He was 55 years of age and had had a winter cough for three years. He had had shortness of breath for six months, anorexia, loss of weight, and sputum which had recently shown traces of blood.

His first X-Rays, (Figs. 6a and 6b), showed dense shadowing and perhaps collapse and cavitation in the left upper lobe. Our suspicions were aroused but he refused bronchoscopy. He agreed, however, to see the thoracic surgeon who advised thoracotomy, but this also was refused. He returned to work and three months later the next X-Ray, (Fig. 6c), showed a system of cavities in the left lung and a diagnosis of tubercle was made, but again he refused to come into hospital or to come off work.

Fifteen months later he was admitted to a surgical ward with upper abdominal pain and died in five days. The X-Ray, (Fig. 6d), showed that the original shadowing in the left lung had cleared but there was now a solid shadow in the right upper lobe. He was written up as dying from hepatic secondaries from a bronchial carcinoma, but no post-mortem examination was done. If we go back to the first film, (Fig. 6a), I think we can see the beginning of this round shadow in the first right interspace.

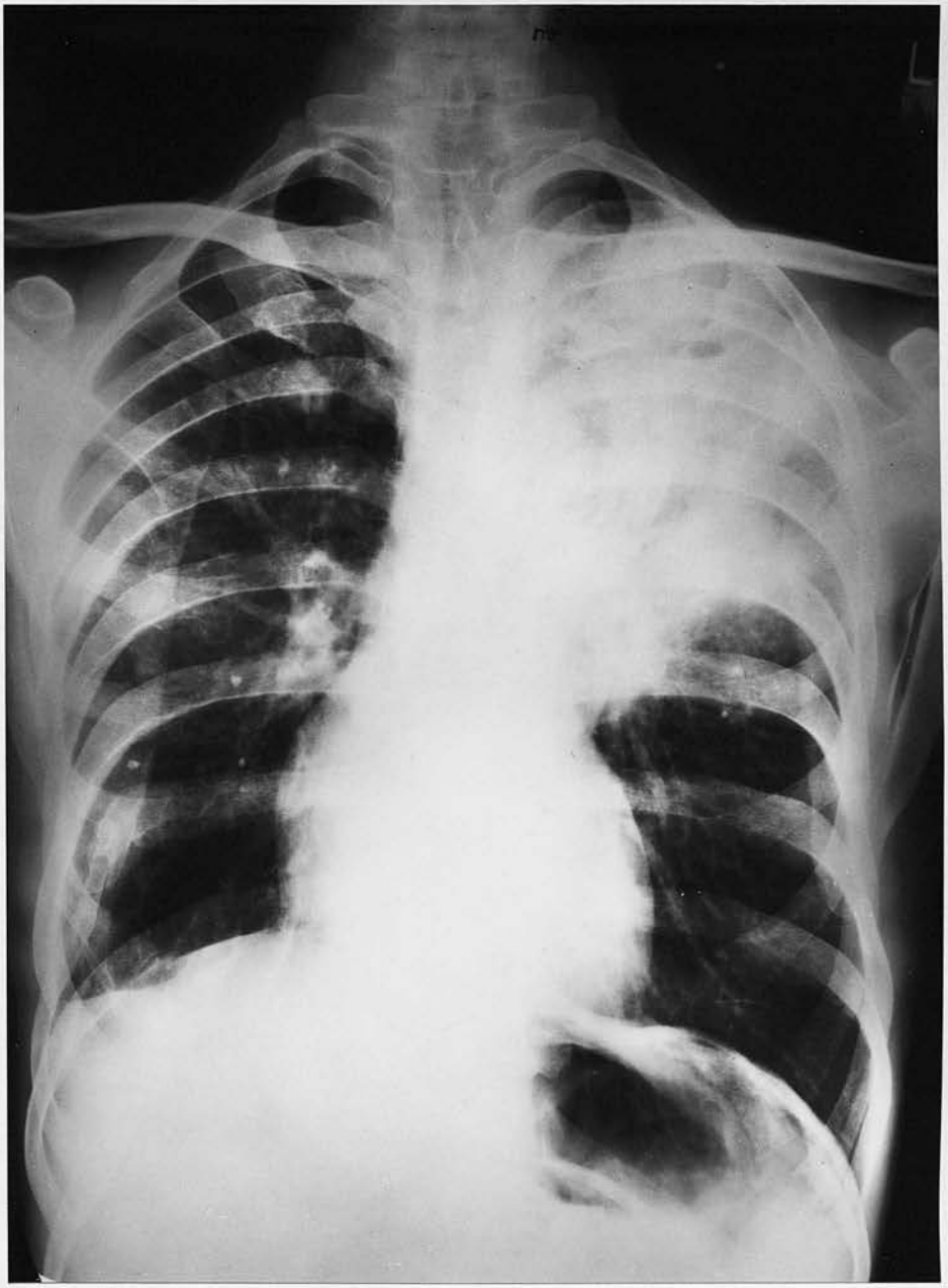

FIG. 6a. - Typical "doubtful diagnosis" case. Certified elsewhere as dying from bronchial carcinoma. ? cough fracture 9th right rib. Male, aged 55, 10-2-55. (Pearson - 1).

FIG. 6b. - Do. 10-2-55.

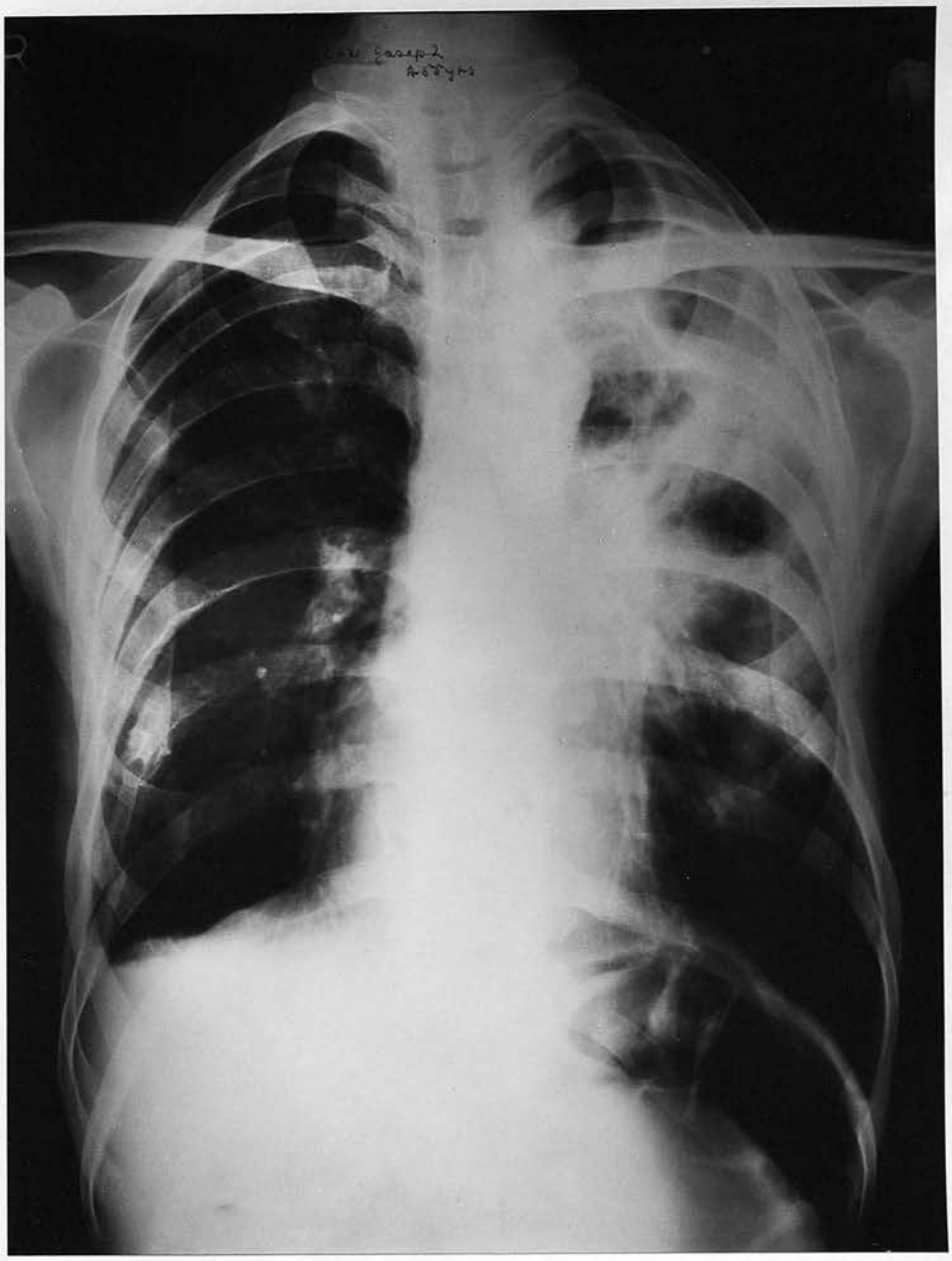

FIG. 6c. - Do. 19-5-55.

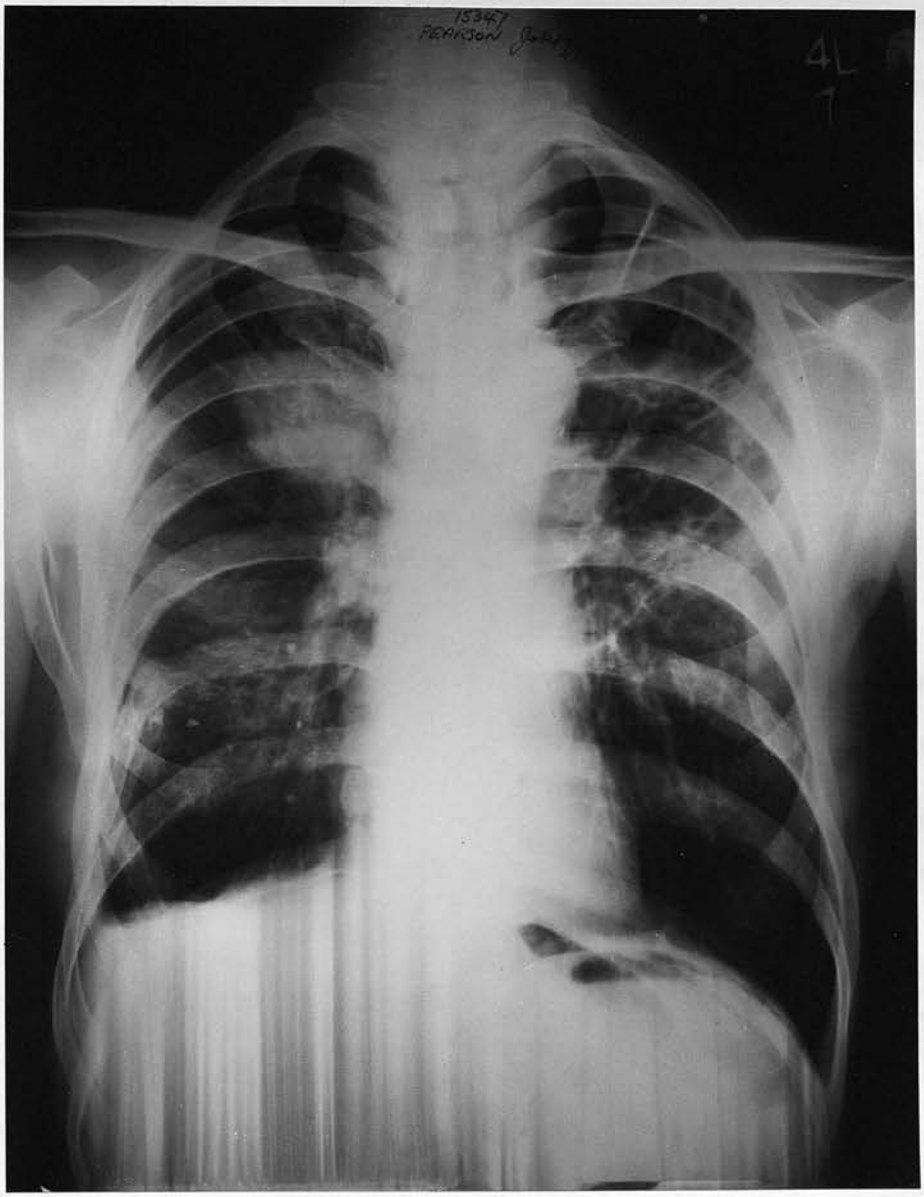

FIGURE 6d. - Do. 31-8-56.

months, not affected by breathing. There were streaks of blood in the sputum. He had ptosis of the right eyelid and Horner's Syndrome was present on the right. For three weeks there had been swelling of the face and neck. He died three days after admission to hospital before any X-Rays could be taken.

Case 5, (Ginger-200), was a similar case in a man aged 57 who died at home from superior vena caval obstruction. He had had a cough since being gassed in 1914, with dyspnoea for three months, and occasional slight haemoptyses for two months. He had had anginal pains for two years and was oedematons, mentally confused, and dizzy. He had subcutaneous deposits over the chest and enlarged axillary glands. He died three days after admission to hospital being too ill to X-Ray even with the portable.

Case 6, (Newton-208), was another case in a man aged 71. He was not a chesty subject. He had had arthritis of the hips for two years and high blood pressure. He had been under his doctor 8 weeks with this when his doctor went on holiday. When his doctor came back he found the patient in bed with acute vena caval obstruction and right heart failure. The patient died at home three days later.

Case 7, (Cookson-226) was another similar case. He was a retired quarryman of 72 who had had bronchitis for two years. He complained of angina on effort for six weeks, loss of weight of one stone, right lower pleuritic pain for two weeks, haemoptysis for one week and ankle oedema. He had dullness

and crepitations at the right base and scattered rhonchi. He died one day after admission to hospital.

It is now proposed to described four other cases, in which though X-Rays were available these all showed only simple effusions. In these cases a cause of death of heart failure, or of carcinomatosis, source unknown, would seem to have been more justified than the one given, (bronchial carcinoma).

The first of these cases, (Holden-7), was a woman aged 73 years, who had had a fissure-in-ano some years before. She had had a chronic cough and sputum for 40 years, but no blood. She had had palpitation for three years and recent dyspnoea. She was admitted to hospital where a large left pleural effusion was found and aspirated several times. It was straw-coloured with 85% monocytes. She died twelve days after admission. On the evidence given she was written up as a bronchial carcinoma.

The second case, (Lord-70), was a man aged 76 who lived alone. He did not seem to be seen very often by his doctor and was emaciated and kept falling. Eventually the neighbours called the police and he was admitted to hospital where he died after two days.

He had gross oedema. His Hb. was 43%, and his R.B.C.s. 3M. He was incontinent and had abdominal pains and diarrhoea. A chest X-Ray the day before he died showed a right basal effusion with or without a lower lobe collapse. He had very little cough or sputum. Haemoptysis was not mentioned. He

was written up as dying from a bronchial carcinoma.

The third case, (Duckworth 186), was a woman aged 61 who had never been chesty although she had had a cholecystectomy 12 years before for gall stones. She had had rheumatic pains in the legs and arms for 8 years. She was fat and pale and had complained of lassitude and shortness of breath for six months. She was admitted to hospital where blood counts showed her haemoglobin to be 55%. Her total white blood count was 15,000 made up as follows:- polymorphs 33%, lymphocytes 27%, monocytes 9.5%, stab cells 15%, and myclocytes and normoblasts 15.5%. Marrow puncture showed a leucoerythroblastic type of anaemia. The spleen was much enlarged. Chest X-Ray at this time was normal.

She was readmitted four months later with swelling of the left knee, vomiting and basal rales. Benzidine and guiac tests were consistently positive. Her chest X-Ray now showed a grossly enlarged heart and small effusions on both sides, but the lung fields were still clear. X-Ray of the pelvis showed disorganisation of the ilia.

She was discharged again and went to live in the country where she died one month later. Apparently the chest symptoms latterly predominated and the cause of death was given as bronchial carcinoma although no fresh pathological evidence was obtained.

The fourth case, (Loynd-244), was a woman aged 66 who also had had gall bladder trouble with attacks of cholecystis for six or seven years. She had had a cough and shortness of

breath with asthmatic attacks for three years.

She was admitted to a surgical ward as an emergency with severe abdominal pain for one week accompanied by vomiting and pyrexia. She was fibrillating at about 100. The abdominal symptoms settled somewhat and her main symptoms were then headache, dyspnoea and left sided chest pain. A chest X-Ray revealed a large left pleural effusion. She died 12 days after admission and was written up as a bronchial carcinoma.

There are two more cases in this indefinite group still to be mentioned.

The first was a man aged 54, (Quinn-72), a painter who had had vague stomach trouble 10 years before and pneumonia five years before.

On 13-3-55 he complained of pain in the left arm and numbness of the fingers. Two weeks later there was some tenderness and swelling on the left forearm so he was given chloromycetin. A week later he was admitted to hospital where X-Rays showed a secondary deposit in the shaft of the left radius, with great destruction, or "rotten post" appearance as shown in Fig. 7a. His chest X-Rays, Figs. 7b, c, showed some vague shadowing at the right base.

The surgeon's diagnosis was either malignant sarcoma of bone, with secondaries in the lung, or secondaries in bone and lung from a visceral cancer.

The patient died three weeks after discharge and as latterly the lung symptoms predominated the general practitioner

FIG. 7a. - Typical "doubtful diagnosis" case. "Rotten post" lesion of left radius, probably a secondary deposit. ? from lung. ? from viscera. Male, age 54, 14-4-55. (Quinn-72).

FIG. 7b. - Do. Chest 14-4-55,
lesion ? primary ? secondary.

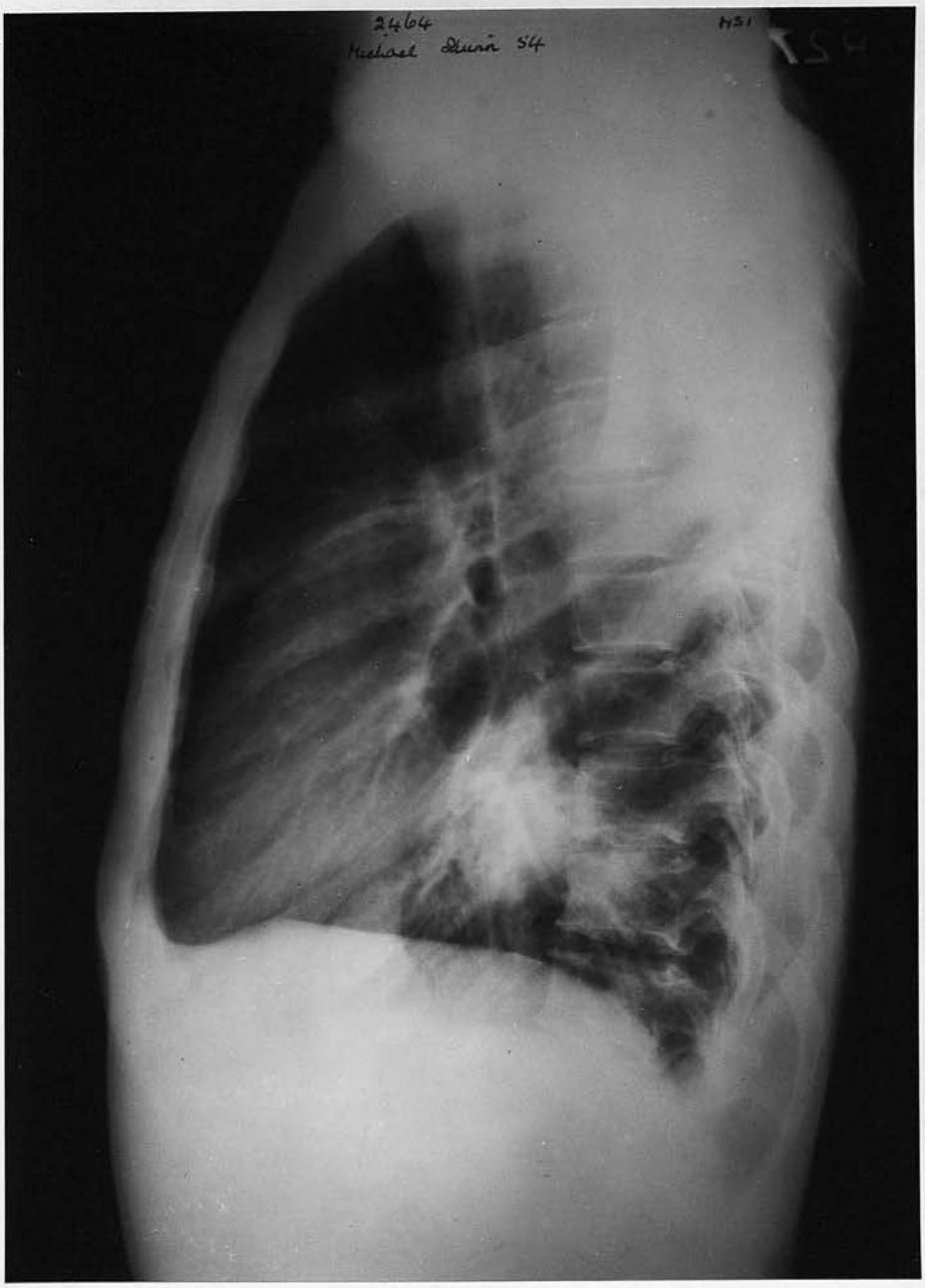

FIG. 7c. - Do. 14.4.55.

wrote up the cause of death as bronchial carcinoma.

The second case still to be mentioned, (Crook-211), was a man aged 62 with a normal chest X-Ray. He had been a blacksmith for 30 years and then a hotel keeper for 15 years.

He had had bronchitis for many years and had been under his doctor for two years. He was off work for 5 weeks before being admitted to hospital for investigation of loss of weight, cough, dyspnoea, and purulent sputum but no blood.

He was febrile with obvious bronchitis and emphysema. He had lost 30 lbs. in weight and his liver was palpable. He was too ill for bronchoscopy but a gland in the left supra-clavicular fossa was excised. This showed trabecular deposits of a very anaplastic carcinoma. The pathologist could not be sure of the source of the cancer. He suggested that it might even be a case of Hodgkin's disease. The diagnosis "used" however was bronchial carcinoma.

Of the 36 doubtful cases we have now described 14.

Another 8 cases are open to considerable argument; four of these might have been certified as dying from heart failure only, two from pneumonia, and two from secondary cancer source unknown.

The remaining 14 cases although deficient in evidence were most probably bronchial carcinomas. The alternative diagnosis was in five cases secondary cancer - source unknown; in three cases tuberculosis; in three cases heart failure; in one case pneumonia; in one case mediastinal cyst, and in one case pulmonary abscess.

These cases illustrate the modern tendency to over diagnose the disease, but they are probably balanced by the two or three cases still being missed altogether (and of which we would hear nothing at all) together with the rejected cases described in Chapter 3 that might have been carcinomas.

Combining Chapters 3 and 4 in Table 5 we have a final rough assessment of the degree of error inherent in the diagnosing of 123 cases of bronchial carcinomas.

254 CASES SUSPECTED AND STUDIED.

123 OF THESE DIAGNOSED AS BRONCHIAL CARCINOMAS.

66 VERIFIED HISTO-PATHOLOGICALLY
21 ACCEPTED AS CONVINCING
36 OPEN TO ARGUMENT.

14 PROBABLY CARCINOMAS
8 DOUBT SLIGHT OR MODERATE
14 DOUBT SERIOUS.

OVERDIAGNOSIS	UNDERDIAGNOSIS
8 CASES WITH SLIGHT OR MODERATE DOUBT.	UNKNOWN NUMBER OF CASES POSSIBLY MISSED ALTOGETHER.
14 CASES DESCRIBED ABOVE	13 CASES LISTED IN CHAPTER 3. P. 36
1 ? TB.	7 NOW DEAD, DIAGNOSIS REJECTED ON VAGUE GROUNDS.
7 NO X-RAYS. ? CARDIAC	6 STILL UNDER OBSERVATION.
4 PLEURAL EFFUSIONS ONLY. PROBABLY CARCINOMAS BUT SOURCE UNCERTAIN.	
1 VISCERAL OR BONE CANCER.	
1 ANAPLASTIC TYPE - SOURCE UNCERTAIN.	
14 to 22. = 10% or more.	13 to ? = 10% or more.

TABLE 5. - Rough assessment of possible error in diagnosing 123 cases of bronchial carcinoma. Perhaps ± 10% or more.

CHAPTER 5

BRONCHOSCOPY

In all 127 bronchoscopies were performed. Of these 42 were on the 131 cases later diagnosed as non-carcinomatous and 85 were on the 123 carcinoma cases. The 85 bronchoscopies were carried out on 61 persons, 16 patients twice and four patients three times.

In these 61 patients positive visual evidence of intralumenary growth was obtained in 40 cases (in six of these cases twice).

Fifty-two biopsies were taken in 44 cases. These were positive in 32 cases (36 biopsies positive). In only one case was a blind biopsy positive for carcinoma. In this case (116) blood could be seen coming from the right upper lobe orifice and a blind biopsy showed an undifferentiated squamous carcinoma.

Thus in 61 cases fit enough for bronchoscopy a tumour was seen in 65% and of that 65% a positive biopsy was obtained in 78%, or 52% of the carcinoma patients fit for bronchoscopy. According to Mayer and Maier, (1956a) up to 60% of bronchoscopies on carcinoma cases may be expected to give a positive biopsy.

Of the total 123 cases diagnosed during the year the percentage bronchoscoped was 50%, the percentage with tumours visible bronchoscopically was 32%, and the percentage with positive biopsy was 26%.

The 32 positive biopsies were classified histologically as 17 squamous (2 female, 15 male), 6 anaplastic (1 female), 6 oat cell (2 female) and 3 adenocarcinomata (all male).

It is surprising that no adenocarcinomata were found among the females, but the numbers are small. In only two cases was a dual pathology reported. One was a female case (239) whose bronchoscopy biopsy suggested an undifferentiated carcinoma. The pneumonectomy specimen suggested an adenocarcinoma. The other was a male case (191) where the bronchoscopy biopsy suggested an adenocarcinoma and a gland biopsy an undifferentiated carcinoma.

Of the 40 cases with positive visual bronchoscopy findings, about 25 had already obvious evidence of metastatic spread, and 5 were over the age of 68, leaving about 15 for consideration of thoractomy. These plus about 10 cases from the negative bronchoscopies made 25 cases or 20% possible starters for thoracotomy.

Among the 21 negative bronchoscopies were six cases in which stricture or bulging was seen and three cases with gross widening of the carina. These findings were a valuable aid to diagnosis.

Table 6 shows that the bronchoscopy cases do not differ greatly in general type from the total cases. If anything they are a little younger, averaging 56 to 58 yrs. compared with the overall average of 61 years. There is not much difference in the duration of symptoms, but the survival period is above average probably because acute fulminating

CARCINOMAS	NO. OF CASES	AV. AGE	DURATION OF SYMPTOMS BEFORE DIAGNOSIS (Weeks)	SURVIVAL AFTER DIAGNOSIS (Weeks)
CASES WITH POSITIVE BRONCHOSCOPY OR BRONCHOSCOPY BIOPSY	40	56	29	27 + 3 Alive
CASES WITH WIDENING OF THE CARINA or stricture	~~3~~ 9	58	31	10
CASES WITH NEGATIVE BRONCHOSCOPY	12	58	49	48 + 3 Alive
ALL CASES	123	61	31	17 + ~~10~~ 9 Alive

TABLE 6. - Comparison between bronchoscopy and total cases.

cases are too ill for bronchoscopy.

It is difficult to correlate bronchoscopic findings with the X-Ray picture, but a review of the X-Rays of the positive and negative bronchoscopies and biopsies is set out in Table 7.

Of the three cases with widening of the carina none were histologically or pathologically confirmed.

Of the 12 carcinomas with negative bronchoscopy, in no case did the X-Ray suggest that the lesion would be bronchoscopically visible. The X-Ray picture in four cases showed hilar masses. In two cases there was upper lobe shadowing, in one case upper lobe collapse, and in four cases peripheral shadowing only. In one (doubtful) case there was lower lobe collapse. Five of these 12 however went forward to major surgery. Bronchoscopy repeated at the surgical centre was still negative in all cases.

A carcinoma of a main stem bronchus may give a variety of X-Ray appearances as shown in Table 8.

Similarly it is not always possible to tell from an X-Ray showing a hilar mass what the bronchoscopic finding is likely to be.

The bronchoscopic findings of 14 cases whose chest X-Rays showed hilar masses are set out in Table 9.

All the three cases showing gross widening of the carina were very advanced and lived on an average only 10 weeks.

Four cases were found at operation to have heavy secondary deposits in the mediastinal glands; yet this was not seen at bronchoscopy. The X-Ray picture of these cases was as follows:-

BRONCHOSCOPY	NO. OF CASES	LESION BRONCHOSCOPICALLY VISIBLE IN								X - RAY					HIST. OF HAEMOP
		RT.				LEFT				HILAR MASS	SHADOWING	COLLAPSE	(EFFUSION also)	PERIPHERAL	
		U	M	L	MAIN	U	LING	L	MAIN						
LESION SEEN	40														
Biopsy pos.	32	3	1	5	7	5	1	5	5	5	3ul 3 m or ll	8ul 13 m or ll	(8)	0	22
neg.	8	1	1	1	1	3	0	1	0	2	3ul	3ul	(1)	0	3
Widening of Carina	3									1		1ul	(1)	1	3
Stricture (neg b'copy)	6	1		2	3					2		1 mark.		3	5
LESION NOT SEEN	12														
Neg. and no biopsy	12									4	2ul	1ul 1LL*	(1)	4	4
	61														~~35~~ 37

* Diagnosis doubtful

TABLE 7 . - Correlation between bronchoscopic and X-Ray findings.

CARCINOMA OF	NO. OF CASES	X - RAY						
		HILAR MASS	COLLAPSE				EFFUSION also	
			WHOLE LUNG	UPPER LOBE	MIDDLE LOBE OR LINGULA	LOWER LOBE	MIDDLE LOBE + LOWER LOBE	
LEFT MAIN STEM BRONCHUS	6		2	1	1	2		(4)
RIGHT MAIN STEM BRONCHUS	8	4		2		1	1	

TABLE 8. - X-Ray appearances of 14 carcinomas of main stem bronchi.

X-RAY	NO. OF CASES	BRONCHOSCOPIC FINDINGS										EFFUSION
		PRESSURE ON	WIDENING OF CARINA	VISUAL LESION SEEN IN								
				RIGHT				LEFT				
				MAIN	UL	ML	LL	MAIN	UL	LING	LL	NEG.
LEFT HILAR MASS	4	Trachea 1	1°									2	1
RIGHT HILAR MASS	10	Rt. Main Bronchus 1		4(3)x		1	2(2)x					2	0
NO. OF CASES	14	2	1	4		1	2					4	1

x Positive biopsies.
o Pleural effusion present early.

TABLE 9. - Bronchoscopic findings in 14 cases whose chest X-Rays showed hilar masses.

1 left hilar mass; 1 collapsed right middle lobe; 1 collapsed anterior segment of the right upper lobe, and 1 collapsed posterior segment of the left upper lobe.

All the three cases showing widening of the carina gave a history of recent haemoptysis, and of the 12 negative bronchoscopies four gave a history of recent haemoptysis. Of the 40 positive bronchoscopies 25 (63%) gave a history of recent haemoptysis.

In two cases of malignant abscess of the upper lobe bronchoscopy was negative.

Of the three carcinoma cases with a negative chest X-Ray unfortunately none was bronchoscoped.

Of the 14 cases among the bronchial carcinoma cases in which bronchoscopy was repeated this was usually within an interval of three weeks. In four cases the diagnosis was obscure and the patients unfit for thoracotomy. The intervals in these cases were 1 year, 13 months, 17 months and 2 years.

Although 127 bronchoscopies were performed only 13 patients went forward to resection. To illustrate the work involved in dealing with these cases one can say that, in the field, for every operated case at least 10 diagnostic bronchoscopies are done.

CHAPTER 6

OPERATED CASES

Out of the 123 carcinoma cases there were 14 thoracotomies done, i.e. 11%. Of these 13 were fit for resection giving a resection rate of 10%.

If we take the 252 cases from which the 123 carcinomas were finally ~~selected~~ diagnosed, 19 were operated on giving a thoracotomy rate of 8%. The figure would be 15% if related to the carcinomas plus exploratory thoracotomies. Of these five were non-carcinomas:- two tubercle, one bronchogenic cyst, one septic suppurative pneumonitis and one a chronic pneumonitis due to the presence of a small foreign body. As stated in Chapter 3 two of the carcinoma cases were undiagnosed before operation.

These figures are very similar to such overall figures as can be obtained for all types of the disease.

In 1954 the deaths from bronchial carcinoma as recorded by the Registrar General were compared with the total operations as estimated by circularising all the members of the Society of Thoracic Surgeons. This gave an overall operative rate of 16.6%. Thoracotomies only were 4.6%, and resections were 12%.

Rosenblatt and Lisa (1956b), give resection rates of 10% to 12% of all cases of the disease throughout America. Special clinics and surgical centres give higher figures. Thus

Bignall (1955), recording 317 cases gave a resection rate of 18%. He states however that many old people may never reach surgical clinics or special hospitals.

American surgeons advocate thoracotomy perhaps more frequently than we do, in the hope of finding really early carcinomas especially peripheral lesions of the coin shadow type.

Thus French et. al. (1956) described 36 thoracotomy cases with a malignancy rate of 11.1%.

Of our 13 resected carcinoma cases 8 had positive bronchoscopy findings before operation, (6 with positive biopsy), and 5 were negative after being bronchoscoped twice. One case, (Westwell-54), illustrated in Fig. 3, had a malignant cavity in the left upper lobe and had shown malignant cells of squamous type, in the sputum, although bronchoscopy was twice negative.

Of the 13 cases seven had no secondary malignant deposits in the regional glands at operation. This figure of 54%, is high. Reinhoff, (1950), found only 30% of cases free, and Nohl (1956) found only 25% free out of 100 resections. On the other hand Overholt, (1949), operating on cases discovered by mass radiography found 75% with no evidence of lymphatic spread.

In our series there were four squamous cell cases in those with glands and four among those without glands.

Nohl, (1956) estimates that mediastinal involvement or infiltration of the perivascular lymphatics or intima is twice

as common with undifferentiated carcinomas as with squamous.

Table 10 shows the findings in the present series but these are too small to be of value. (I would like to analyse say 500 operated cases in this way).

Holmes Sellars, (1955), and Walter and Pryce, (1955a), state that squamous cancers which grow slower, more centrally, and metastasise slower than the other histological types form a higher percentage of operated cases than of all cases as judged by post mortem findings. This problem is discussed again in Chapter 8.

The presence of secondary deposits in mediastinal glands at operation has a VITAL influence on the prognosis as will be seen from Table 11. Thus Bignall and Moon, (1955), state that, of 100 cases known to be without regional metastases, the 5 year survival rate was 48%. Of 133 cases known to have metastases the rate was 11%. In our series, as will be seen from Table 10, of the 7 cases without secondary deposits one has died, and one is not well, but five are well and working giving an 86% two year survival rate, while of the 6 cases who had involvement of the local glands 5 are dead and the single surviver is very ill.

It is however not possible to tell preoperatively whether the mediastinal glands are going to be involved or not.

Comparing the pre-operative findings of the two groups with and without regional spread, no difference could be detected. With regard to age the former group averaged 56

OPERATED CASES	CASE NO.	MALE FEMALE	AGE	DURATION OF SYMPTOMS (WEEKS)	HIST. TYPE	2 YRS. FOLLOW-UP	SURVIVAL AFTER DIAGNOSIS (WEEKS)
A. Without metastases in regional glands	127	M	52	26	Adeno	well & w.	
	128	M	59	6	Sq.	well & w.	
	131	M	51	39	Undiff.	died	87 weeks
	145	M	46	8	Sq.	well & w.	
	154	M	51	104	Sq.	well & w.	
	221	M	60	32	Sq.	died	14 weeks
	264	M	52	52	Adeno	well & w.	
			Av.53	Av.38			
B. With metastases in regional	13	M	56	12	Sq.	died	84 weeks
	17	M	58	3	Sq.	died	30 weeks
	54	M	54	150	Sq.	Ill	
	93	M	68	38	Sq.	died	15 weeks
	102	M	46	6	Ana-plastic	died	32 weeks
	239	F	56	9	Adeno	died	38 weeks
			Av.56	Av.36			

TABLE 10. - Mediastinal gland involvement of the 13 operated cases.

AUTHOR	SURVIVAL OF OPERATED CASES					
	WITH REGIONAL GLAND METASTASES			WITHOUT R.G. METASTASES		
	NO. OF CASES	2 yrs.	5 yrs.	NO. OF CASES	2 yrs.	5 yrs.
Bignall & Moon 1955.	133	27%	11%	100	61%	48%
Present series	6	17%		7	86%	
Oswald 1956.						50%
Gifford & Waddington 1957.	97	26%	8%	184	60%	33%
Taylor and Waterhouse 1950.	1147					30%

TABLE 11. - Survival rates of operated cases with and without metastases in the regional glands.

years, the latter 53; the average for all the 123 carcinomas being 61 years.

With regard to duration of symptoms before diagnosis the group with glands averaged 36 weeks and the other group 38 weeks, compared with an overall average of 31 weeks for all the carcinomas.

There was no evidence of a differing pattern when the two groups were compared with regard to symptoms or signs. Two of the cases without glands had complained of pain, one for eight months. Half of each group had had haemoptysis; among the no-gland cases haemoptysis had been present in four cases for 2 years, 9 months, eight weeks and six weeks. ~~One~~ Two of the no-gland cases however ~~was a~~ were mass radiography pickups, and one of the gland cases had a palpable liver. Perhaps, although there was no difference in weight, pain, cough etc. the gland cases had slightly more evidence of systemic upset such as headache, tachycardia, fever and joint pains, and more of them felt ill.

With regard to bronchoscopy there was, as described at the beginning of this chapter, no difference in the two groups.

With regard to histology there was likewise no difference. The no-glands group contained four squamous, two adeno carcinomas and one anaplastic. The gland group contained four squamous, one adeno carcinoma and one anaplastic.

As stated earlier in this chapter this seems a slightly unusual finding. The extent of the X-Ray changes was similar in both groups, perhaps a little more hopeful in the no-gland

group. This group contained two peripheral lesions, two with lobar collapse, two infiltrative lesions and one hilar mass. The gland cases showed no peripheral lesions, three showed lobar collapse, one was an abscess and two were hilar masses.

With regard to glands visible on preoperative X-Rays however there was thought to be a difference between the two groups. Root glands were suspected in the p-a films of five out of the six malignant gland group, and what were thought to be malignant glands were seen in the lateral X-Ray in all six of this group.

In one out of the seven cases comprising the non-malignant gland group, however, root glands were thought to be seen pre-operatively in both p-a and lateral X-Ray films. In this case mediastinal glands were removed at operation. In another case clearance of para-tracheal glands was carried out as they looked malignant. In the other five cases of the non-malignant group glands were removed at operation for histological examination.

Thus it seems that while malignant glands can very frequently be seen on p-a, and lateral X-Rays, non-malignant enlarged glands may occasionally also be visible radiologically. Similarly the tumour itself or segmental collapse of the lung may complicate the interpretation.

The seven cases found free from glands at operation represent less than 6% of the total 123 carcinoma cases.

The selection of these 7 cases is shown in Table 12. Of the 123 cases 90, i.e. 72% had clinical signs of metastases on

123 CASES OF BRONCHIAL CARCINOMA	NO. OF CASES	% OF TOTAL		
OBVIOUSLY UNFIT FOR SURGERY BECAUSE OF METASTASES	81	65%		
REJECTED BECAUSE OF PRESUMPTIVE SIGNS OF METASTASES	9	7%		
REJECTED BECAUSE OF HEART DISEASE, EMPHYSEMA, DYSPNOEA ETC.	5	4%		
REFERRED TO THORACIC SURGEON	28	24%		
REJECTED AFTER ASSESSMENT			9	
REJECTED AFTER ADMISSION TO THORACIC SURGERY UNIT			2	
REFUSED SURGERY			4	
THORACOTOMY ONLY			1	
RESECTED			13	
FOUND TO HAVE SECONDARY DEPOSITS IN MEDIASTINAL GLANDS				6
FREE FROM SUCH GLANDS				7

TABLE 12. - Assessment of 123 Cases of bronchial carcinoma for surgery. (See Chapter 9 for analysis of the cases with metastases).

first diagnosis. Five (4%) were obviously unsuitable for surgery for other reasons.

In all 29 (24%) were referred to the thoracic surgeon. Nine of these were rejected after assessment chiefly because of presumptive evidence of spread of the carcinoma or because of emphysema and shortness of breath. The actual reasons are listed as follows:-

1. Liver enlarged. Anorexia. Pain.
2. Gross tumour bronchoscopically. Pain.
3. Dysphagia. Pleural effusion. Mediastinal gland.
4. Gland biopsy showed undifferentiated carcinoma.
5. Coronary thrombosis one year before. Great broadning of the carina.
6. Liver enlarged. Dysphegia. Pain.
7. Chronic bronchitis and emphysema.
8. Do.
9. Paratracheal gland on X-Ray. Anorexia. Nausea. Vomiting.

A further 2 cases were rejected after admission to the Thoracic Surgery Unit and one after thoracotomy. Four considered fit for surgery refused operation.

Sir Clement Price Thomas, (1955), has stated that 70% of cases are beyond surgical aid when they arrive at the surgery clinic. If we include the cases that are obviously too ill for surgery when first seen, I think the percentage goes up to 80% or 85%.

CHAPTER 7

NECROPSIES

Of the 123 cases of bronchial carcinoma occurring during 1955, 113 are now (30.9.57) dead. Of the deaths 63% (71 cases) occurred at home and 37% (42 cases) in hospital.

Only one necropsy was carried out on the patients dying at home, this was a war pensioner. Of the 42 cases dying in hospital necropsies were carried out on 18, i.e. on 43% of the carcinomas dying in hospital, but on only 16% of the total deaths.

The post mortem cases are quite sharply divided into two main groups.

THE FIRST GROUP, consisting of 10 of the 19 cases, consisted of old ill patients dying of acute disease after an average stay in hospital of only 11 days. Their average age was 64 years and their average period of survival after being seen for the first time by the consultant staff was 3 weeks. None of these cases had been bronchoscoped and one was too ill even to X-Ray. The object of the necropsies in this group was to discover the diagnosis.

THE SECOND GROUP consisted of 9 patients in whom the diagnosis had been made on an average 25 weeks before. They were mostly readmissions to hospital. Their average age of 59 years was less than the first group. Four of them had previously had a bronchoscopy which had been negative. One had been operated on and one had also had tuberculosis with a

positive sputum. In one case, a war pensioner, the necropsy was ordered by the coroner, in the remaining eight the post mortems were requested by the physicians out of interest.

I would like to mention three cases in the first group as they show how bronchial carcinomas may present clinically as acute fatal illnesses of apparently short duration.

The first of these was a man aged 60, (Rigby-110), who had been a little chesty since having a duodenal ulcer operation 20 years before. He had been off work only three weeks although he had complained of cough, loss of weight and shortness of breath for six months. He had not coughed up blood. On admission to hospital he had a grossly enlarged liver, oedema of the ankles and sacrum and rales and rhonchi over both lungs. He died on the third day after admission without being X-Rayed, and a post-mortem examination was considered necessary to verify the diagnosis. This revealed a bronchial carcinoma in the right lower lobe with secondaries in the liver. Histology showed it to be very anaplastic.

The second case in this group was a man aged 58 (Rylett-38) who had been well and working till six weeks before. On admission to hospital he was found to have an enlarged liver, dyspnoea, clubbing and loss of weight. He had had a cough and one ounce of sputum for about six weeks, but no blood. He had had low back pains for about three weeks. His chest X-Ray revealed collapse of the whole of the right upper lobe with paralysis of the right cupola. He died two weeks after admission. A post mortem was considered necessary. This

revealed a bronchial carcinoma with metastases in liver, supra renals and spine.

The third case, (Gillibrand 115), was a man aged 61, who was brought to the hospital in an ambulance and admitted from the out-patient department. He died three days later. Fig. 8 shows his chest X-Ray two days before he died. He gave a short history of only two months, with weakness and cramp in the legs, staining, loss of weight and shortness of breath. He complained of a great insatiable thirst. He had been gassed in the first world war and had worked testing on aero-engines for 10 years. He had smoked 30 cigarettes a day all his life. The X-Ray did not show very advanced changes but the necropsy revealed a carcinoma in the right lower lobe with secondaries in the liver and spleen. There was an enormous secondary deposit in the left suprarenal gland which weighed 11 ounces. There was also a deposit in the right suprarenal which weighed 1½ ounces.

In only three of the necropsies was histological confirmation obtained, and generally speaking the post mortem reports were brief with mention only of the usual commonest metastatic sites.

In two cases no secondary deposits were found. In one of these, a man aged 78, (Billington-243), with a long history of chronic bronchitis and emphysema and a rather indefinite X-Ray, whitish areas were seen in the right lower lobe and some enlarged glands were present. A diagnosis of bronchial carcinoma was made in spite of the fact that three sections showed consolidation of

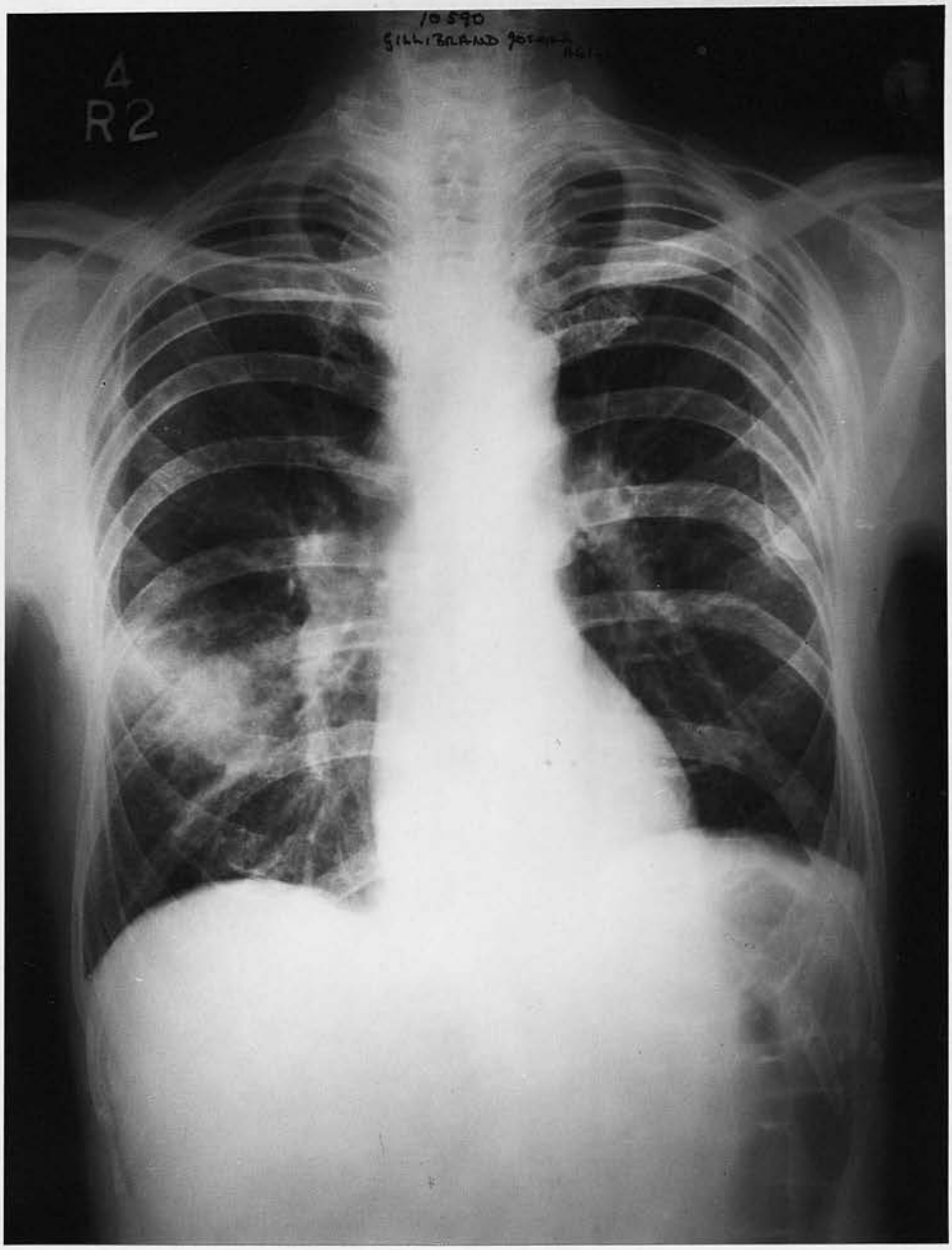

FIG. 8. - Chest X-Ray, two days before death, of a case of Addison's disease due to bronchial carcinoma.
Male, age 61, 23·6·55.
(Gillibrand - 115).

pneumonic type and no evidence of malignancy. In the other case, a man of 72, (Smith-182), illustrated in Fig. 5, a tumour was undoubtedly present in the right lower lobe and he was also found at post mortem to have a ~~pneulent~~ purulent pericarditis. In the absence of secondary deposits and histology we were not sure whether this was a bronchial carcinoma or not.

Any case showing a solitary lesion requires histological confirmation. Even where there is obvious tumour formation and involved glands it is often extremely difficult at the post mortem to be sure it is a primary bronchial carcinoma and to decide the point of origin of the growth which may have spread into both lungs and many of the glands. Thus even in pulmonary specimens resected at operation Walter and Pryce, (1955b), could be certain of the site of origin in only 59% of cases. In addition to the common secondary intra-pulmonary metastases from breast, bones, kidney, prostate, thyroid, ovary and stomach cancers Liebow, (1952), states that an isolated metastasis of kidney or colon may centre about, and even invade a bronchus so as to suggest a primary lesion. Seiler, Claggett, and McDonald, (1950), reviewed 52 cases from the literature and reported 10 from the Mayo Clinic of metastatic malignant tumours suitable for resection. Gross bronchial involvement was demonstrated in 7 of their cases, in four of which bronchoscopic biopsy was positive. Probert, 1956, described three cases of bronchial invasion by adenocarcinomas of intestinal origin. In one of these cases a lobectomy and also a recto-sigmoid resection was carried out. In a second case a colonic re-

section and three years later a left pneumonectomy ~~was~~ were done. In this case after another three years small metastases were suspected in the right lung but the patient was still at work. This illustrates how slowly a colonic tumour may grow. Any such case with a metastasis causing bronchial obstruction could be regarded as a primary bronchial carcinoma in the absence of good histology.

Smithers, (1953) gives two examples of a wrong necropsy diagnosis in the absence of histological examination in the records of the joint consultative clinic of the Brompton and Royal Marsden Hospitals.

In three cases in our non-carcinoma controls a post mortem verdict of tuberculosis had been queried because, in the absence of histology, bronchial carcinoma was considered a possibility. (Lyons 238, Aspden 28, and Bowker 179).

Thus histology is just as important to prevent over-diagnosing the disease as to prevent under-diagnosing it.

In view of the increased number of necropsies being done all over the country, Fullerton, (1956), feels that the real increase in the deaths from lung cancer may not be so great as the figures suggest.

She found that the percentage of necropsies carried out in her hospital had increased from 36.1% of the deaths for the period 1947-1949 to 61.7% for the period 1950-1952. During the first period there were 37 cases of bronchial carcinoma, in the second period there were 59 cases of which 22 were unsuspected

before death.

In the present series of 19 necropsies (16% only of the total 123 cases) the diagnosis had been in serious doubt clinically in 10 cases, but these were all in the acutely ill older age group described above. They were not known to the consultant staff prior to admission to hospital where they died after an average stay of 11 days. Their average age was 64 years. It will be seen therefore that this group is either very rapidly progressive or else most tardily referred to the hospitals. I agree with Fullerton that cases in this group were probably frequently missed in the past. The average age of her undiagnosed cases was 64 years.

Spicer, 1956, states that in the period 1929-1946 the post-mortem records of two London teaching hospitals showed a wrong diagnosis of bronchial carcinoma of 1 : 3.

Are bronchial carcinomas, as a proportion of all carcinomas found at necropsy increasing? Rosen-Glatt and Lisa (1956a), give most of the early figures from which Table 13 is compiled. They state that in general there has been a steady increase in bronchial carcinomas as a proportion of all carcinomas found at necropsy. They admit however that some of the early pathologists, notably Junghanns of Dresden, recorded a surprisingly high percentage of primary lung cancers, and that the increase shows a less striking change than might be expected from the recorded death rate.

AUTHOR	CENTRE	PERIOD	NO. OF AUTOPSIES	PRIMARY LUNG CARCINOMAS AS % OF ALL CARCINOMAS MALE AND FEMALE
JUNGHANNS[o]	DRESDEN	1898 - 1902		11.62[x]
"	"	1912 - 1917		13.58[x]
"		1918 - 1922		16.58[x]
STEINER[o]	CHICAGO	1901 - 1941	5515	10.3[x]
JAFFLE[o]	VIENNA	1915 - 1918		10.73[x]
MAXWELL AND NICHOLSON[o]	BARTS.	Prior to 1914		10
DOLL 1953	LEEDS	1928 - 1932		7.5[x]
"	LEEDS	1949		16.9[x]
DAFF ET AL. 1951	BARTS.	1930 - 34		23.3[x]
	"	1945 - 48		31.0[x]
CLEMMESEN 1954	MATZ	1927 - 37		13.7
"	STEINER	1901 - 1943		7.6
"	"	1918 - 1946		8.4[x]
"	KLOTZ	1926 - 1936		17.0

x = Cancers not carcinomas. o = Quoted by Rosenblatt and Lisa (1956a).

TABLE 13. - Bronchial carcinomas as a percentage of all carcinomas found at autopsy.

In Table 13 the figures of Junghanns are very significant if we can be sure that they represent bronchial carcinoma as we know it today. His figures and those of Steiner and Jaffe give a percentage of lung cancers to all cancers at post-mortem much in excess of the percentage of deaths from lung cancer to deaths from all cancers as recorded by the Registrar General for 1925 and the previous years.

The former figure varies from 10% to 16% while the latter works out at only 4%. (Table 31).

The percentage of lung cancer deaths to all cancer deaths for 1955 works out at 18.5% (Table 31). This great increase has not been paralleled in the post mortem studies.

Does this mean that the disease was prevalent in the pre 1925 era if looked for at post-mortem, but that it was not being found clinically?

I would have liked to have been able to compare the necropsy histology with the operative histology but in the field the former is not done as a routine. In conjunction with an epidemiological survey, if it were to be complete, there would need to be a very high proportion of necropsies with routine histology.

CHAPTER 8

HISTOLOGY

Unfortunately the nearer one approaches to obtaining all the cases of bronchial carcinoma occurring in a given area the smaller becomes the percentage histologically confirmed. Thus of my 123 cases histological confirmation was available in only 49 i.e. 40%.

When assessing the histological type of a bronchial carcinoma unless adequate well-fixed material is available the pleomorphism encountered makes it extremely difficult to be accurate. Similarly the autolysis in post-mortem material is also a drawback and Walter (1957) found a number of cases in which it was just not possible to say what sort of tumour it was, due to the poor preservation of the cells.

Another snag described by the histologists is Bratten's artefact in bronchial biopsies, where distorted lymphocytes take on the appearance of oat cells.

Walter and Pryce (1955) in a study of 207 surgical specimens and 159 necropsies did not meet any truly mixed growths and they concluded that the main difficulties in classifying cancer of the lung are due either to changes such as squamous metaplasia or to differentiation of the oat-cell growths, which they believe constitute a less malignant group than the true undifferentiated.

Kirklin et. al. (1955) at the Mayo Clinic (as shown in Table 16) record a rather low percentage of squamous cases (34%); many cases that others might have called poorly differentiated squamous have been placed in the anaplastic group, along with the small oat-celled group, which in their series gives the lowest 5 year survival rate.

Unfortunately my squamous group is rather loosely classified. Thus in four of my cases the histological report stated"anaplastic squamous". Although this might mean squamous metaplasia in one of the other groups they have been classified as squamous.

I have had to combine the oat-celled with the undifferentiated or anaplastic cases in one group. Two of the latter were queried as possible sarcomas.

My third group is the adeno-carcinoma group. As pointed out by Mayer and Maier (1956), the inclusion of even a small number of adenomata with this group would give a completely misleading impression as to the prognosis. Their five year survival rate of adenocarcinomas was almost as good as with squamous carcinomas.

I have no case of alveolar cell (or terminal bronchiolar) carcinoma.

Two of my undifferentiated group were queried as possible sarcomas. One of these, a man aged 43 appeared to run a normal course but histology at necropsy showed a very aplastic lesion with mitosis and giant cells. The other, a woman aged 48 presented with an intercostal lump of brain-like consistency.

The subsequent course was of a bronchial carcinoma of the left main bronchus and she survived 43 weeks. The histology, however, showed "a breaking down malignant tumour, showing some polymorphism. Is it a primary in the breast? Shall class among the sarcomas although melanoma should be considered."

Table 14 shows the 49 confirmed cases divided into the three groups, squamous, adenocarcinomas and undifferentiated. The type was ascertained as follows:- by bronchoscopy biopsy 32 cases, operation histology 13 cases, necropsy histology 5 cases, examination of sputum for malignant cells 3 cases, biopsy 4 cases (1 abscess, 2 gland, 1 skin), and thoracotomy 1 case.

Sputum was sent for examination for cancer cells in only six cases. Three were positive and three negative. No false positives were obtained. Schuster (1955), states that between 60% and 80% of pulmonary cancer patients have recognnisable malignant cells in the sputum.

In one case, (Westwell-54-Fig. 3), sputum examination in between two negative bronchoscopies showed cancer cells of squamous type. This was later confirmed by operation histology. The lesion was a small malignant abscess in the posterior segment of the left upper lobe.

In two cases malignant cells were considered to be present in pleural fluid. This was used as confirmatory evidence only as it had been found that among the non-cancer cases, some ambiguous reports of cancer cells in pleural fluid had been obtained. (See Chapter 13, P. 5).

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HISTOLOGICAL TYPE	SEX	NO. OF CASES	AV. AGE	UNDER 50 YRS.	DURATION OF SYMPTOMS BEFORE DIAGNOSIS (WEEKS)	NO. RESECTED	TOTAL 2 YR. SURVIVORS (ALL WERE RESECTED)	DUR. OF SURVIVAL FROM DIAGNOSIS (WEEKS) (NON OPERATED ONLY)	SYMPTOMS ON FIRST DIAGNOSIS		EVIDENCE OF METASTASES ON FIRST DIAGNOSIS
									PAIN	HAEM	
Squamous	Male	26	58	3	38	8	4	26	9	11	15
	Female	4	63	1	68	0	0	21	0	1	3
Adeno	Male	4	60	0	31	2	2	49	3	2	1
	Female	1	56	0	9	1	0	38	1	0	1
Undifferentiated	Male	11	49	5	19	2	0	18	3	8	10
	Female	3	56	0	22	0	0	28	1	1	2
Total	Male	41	56	8	32	12	6	26	15	21	26
	Female	8	60	1	43	1	0	26	2	2	6
	All cases	49	57	9	34	13	6	26	17	23	32

TABLE 14. - Incidence of histological types by age, sex, duration of symptoms, survival, etc.

Although the numbers are small, Table 14 bears out the findings of Rosenblatt and Lisa (1956d), that the female squamous cases show a higher age group than the male squamous. It ~~also~~ possibly suggests, as has been indicated by Bignall (1955), and Nicholson et. al. (1957), a greater proportion of undifferentiated cases among females. There was no excess of adenocarcinomas among females, although the incidence has been put as high as 58% in female necropsy series by Rosenblatt and Lisa (1956d).

Table 14 suggests an excess of undifferentiated cases in the male under 50 group. Among younger persons generally the squamous type is stated to be less common, and the adenocarcinomas and undifferentiated types correspondingly increased (Lancet 1956). Rosenblatt and Lisa (1956e) describe 25 cases of bronchial carcinoma from the literature in persons of 20 years and under, in which the histology is known. Only three of these were of squamous type.

Table 14 also shows the incidence of pain and haemoptysis as presenting symptoms among the three main histological types. No pattern seems to emerge, and this is the impression also with regard to the extent of the X-Ray changes on first diagnosis.

Table 14 suggests, however, that the presence of metastases on diagnosis, and the subsequent course of the disease may vary with regard to histological type, at least as far as the anaplastic group is concerned, 12 out of 14 cases having metastases on diagnosis, and the survival period for both operated and non-operated being very poor.

Both the undifferentiated cases that were operated on have since died. One of these, (Roxburgh-102), was at first thought to be free from metastases although he had had some chest pain. Pneumonectomy however was carried out with great difficulty because of an abnormally large growth involving the pericardium and great vessels. Hilar and paratracheal glands were involved. He died after 15 weeks. In the other case (Tomlinson-131), at right upper lobectomy, there was no evidence of secondaries in the regional glands. After a spell of light work, however he developed secondaries in the liver and died. One might wonder whether if bronchoscopy biopsy shows an anaplastic cancer operation is worth while. However as shown in Table 16, of Bignall and Moon's 5 year survivors 19% were of the undifferentiated type.

Table 14 gives an estimate of the duration of symptoms before diagnosis for the three main types. This is a somewhat unreliable figure as will be explained in Chapter 9, but perhaps the figures do correspond with the relative rates of growth of the cancers, the undifferentiated being, on average, quickest to come to investigation and diagnosis.

All the non-operated of the 49 histologically confirmed cases are now dead, the average period of survival from the time of first diagnosis being shown in Table 14. The numbers are too small to allow of very firm conclusions, the male squamous cases seemed however to survive longer than the male undifferentiated.

The number of adeno-carcinomas in the present series is only 5. In spite of the fact that four of these had pain on

first diagnosis, and two of them haemoptysis, the survival record was relatively good. Of the three operated cases one died after 38 weeks, but the other two are well and working after two years. Both of the non-operated cases survived nearly a year.

In all, 4 cases with malignant abscesses or cavities were met with. In the one case with known histology this was squamous.

Table 15 shows an attempt to divide various groups of carcinomas into the three main histological types. This is a very important but extremely difficult thing to do and this attempt is seriously biassed in five ways.

1. The histology itself is probably not 100% accurate.
2. Only 49 out of 123 total cases are represented.
3. More bronchoscopy biopsies were done among the fitter patients.
4. It contains all the operated group.
5. Terminal fulminating cases were not bronchoscoped, and only 5 out of 19 necropsies were completed with histology.

As the numbers in my series are very small I have in Table 16 compared them with a number of large series. These show a gradual increase in the proportion of squamous cases and a corresponding reduction of the proportion of undifferentiated cases in the following groups:- necropsy, unfit operation, total cases, operated cases and 2, 3, and 5 year survival groups.

Table 16 shows that necropsy cases as opposed to operation cases show a reduction in the squamous group from 60% to 20% and an increase in the undifferentiated from about 24% to 48% and an increase in the adeno-carcinomas from 15% to 28%.

			% of Col. 1	% of ~~Total~~ Total of known histology	
Total Cases	49	Squamous	30		61%	
		Adeno	5		10%	
		Undiff.	14		29%	
Resected	13	Squamous	8	(61.5%)	16%	26% of squamous
		Adeno	3	(23%)	6%	60% of adeno
		Undiff.	2	(15.5%)	4%	14% of undiff.
Unfit resection	36	Squamous	22	(61%)	45%	
		Adeno	2	(5.6%)	4%	
		Undiff.	12	(33%)	24%	
1 yr. survivors	13	Squamous	6			
		Adeno	3			
		Undiff.	1			
		Unknown	3			
2 yr. survivors	~~8~~ 9	Squamous	4			
		Adeno	2			
		Unknown	3			

TABLE 15. - Histology of operated and non-operated groups and of one and two year survivals. (In only 49 of the total 123 cases was the histology known).

Group	No. of Cases	Squamous	Undiff.	Adeno.
Necropsies				
Walker & Pryce 1955	159	20%	48%	28%
Bignall 1955		20%	66%	
Cases unfit for operation				
Present series	36	61%	33%	6%
Total cases				
Present series	49	61%	29%	10%
Bignall 1955		50%	33%	
Nicholson et. al. 1957	414	56%	37%	6%
Mayo Clinic, Kirklin et. al.		34%	53%*	13%
Operated cases				
Present series	13	62%	15%	23%
Walker & Pryce 1955	207	60%	24%	16%
Bignall & Moon 1955	453	61%	26%	13%
Nohl 1956	100	59%	31%	10%
Nicholson et. al. 1957	191	69%	20%	11%
Gifford & Waddington 1957	347	55%	34%	9%
Follow-up				
Present series 2 yrs.	6	67%	0%	33%
Nicholson et. al. 1957 3 yrs.		85%	4%	10%
Bignall & Moon 1955 5 yrs.°	153	65%	19%	16%
Gifford & Waddington 1957 5 yrs.		91%	9%	0%

* Large cell 38%, small (oat) cell 15%.

° In this series there were initially twice as many undifferentiated cases than adenocarcinomas.

TABLE 16. - Distribution of histological types among various groups of bronchial carcinomas.

Operation cases account for only 10% of the total, and, even with the other cases fully investigated during life, account for only a third of all cases (as in this series). ~~the~~ Necropsy figures are Therefore sometimes considered as more representative of all cases of representative lung cancer.

Holmes Sellors (1955) states that if we accept this view the operability rate for squamous cases is infinitely superior to that of other cell types. The increased incidence of undifferentiated carcinomas and to a lesser extent of adenocarcinomas at necropsy suggests that both of these are unfavourable for surgery.

It is important that the proportion of each histological type in all carcinomas be worked out, as it could be in a survey of this type provided adequate histological confirmation of the non-operated cases could be arranged.

Bignall (1955) considers that necropsy estimates may be biased in favour of the more malignant growths, those causing death before diagnosis or producing a rapidly fatal illness. Thus half of the necropsies in this series were done on undiagnosed cases and very few necropsies indeed were done on cases where the histology had been investigated during life.

On the other hand operation cases may contain too few of the more malignant types. The intermediate group, i.e. cases found unfit for operation after full investigation, may be significant. In my very small series they contained 61% of squamous cases, the histological types being distributed more like the operation than the necropsy series.

CHAPTER 9

SYMPTOMS AND SIGNS, AND EVIDENCE OF METASTASES ON FIRST DIAGNOSIS

In this study I am interested in symptoms and signs only in so far as they indicate the course of the disease and the stage at which diagnosis takes place.

The main question is whether the symptoms and signs suggest the lesion to be invading tissue either directly or by metastases.

Rosenblatt and Lisa (1956f), examining the admission complaints of 210 cases later verified at necropsy estimated that at least 42% of INITIAL symptoms were due to metastases as shown in Table 17.

In Table 17 we may accept such symptoms as dyspnoea, pain, headache, vertigo, hoarseness and vomiting as indicative of secondaries because ~~of existing~~ the exciting cause was subsequently checked by post-mortem examination. But at the time of first diagnosis, these same symptoms or signs would only warrant a suspicion of secondary spread.

Similarly such symptoms and signs as cachexia, oedema, Addison's disease, haematuria, mediastinal glands thought to be visible on the X-Ray, paralysed diaphragm, aphonia, bronchoscopic widening of the carina, dysphagia, Horner's syndrome, vena caval obstruction, auricular fibrillation, backache, sciatic pain, neuritis, foot drop, wasting of muscles of the

SYMPTOMS		CASES
1. Pain		
Thoracic	24	
Shoulder	9	
Back	8	
Epigastric	4	
Sciatic	3	
Arm	2	
Hip	1	
Neck	1	52
2. Dyspnoea		13
3. Extremity Weakness		7
4. Cerebral		
Headache and Vertigo	4	
Drowsiness	2	
Hemiparesis	1	7
5. Subcutaneous Mass		
Neck	2	
Chest	1	
Groin	1	4
6. Hoarseness		4
7. Facial Oedema		1
8. Vomiting		1
Total Cases		89

Table 17. - Initial symptoms considered to be due to metastases on the evidence of later necropsy findings among 210 cases.
(Rosenblatt and Lisa 1956f).

arm or hand, anorexia, enlarged liver, jaundice, effusion, extreme thirst, enlarged spleen, hemiplegia, cerebellar symptoms, ataxia, ptosis, blindness, facial palsy, diplopia, mental confusion, dementia, convulsions, arm paresis, paraesthesia, facial palsy, epigastric pain, and secondary deposits in bones especially ribs, vertebrae, pelvis, skull, sternum, clavicle or humerus, skin nodules or masses, or enlarged lymph glands, supraclavicular, axillary or in the groin, could only make us suspicious in varying degree of the presence of metastases.

If however the diagnosis is confirmed bronchoscopically or by biopsy or even if the history, clinical findings and X-Rays are straight forward, then these symptoms and signs will more strongly infer metastases. Their presence may be confirmed at operation, or by biopsy or by a post-mortem if the course of the disease is short. Even in the absence of a post-mortem examination if the disease is fulminating, and dual pathology can be reasonably excluded, initial symptoms suggestive of metastases may be accepted as such.

In accordance with this reasoning I have, in Table 18a tabulated against each of my 123 cases some of the evidence available regarding the present of metastases on first diagnosis.

This Table of course contains the 36 (c11) cases in which the diagnosis is open to varying doubt. These could not be omitted however or the overall picture would have been lost.

CASE NO.	CLASS	AGE	HIST.	DURATION OF SYMPTOMS BEFORE DIAG. (WEEKS)	EVIDENCE OF METASTASES	DIAG. CON-FIRMED BY	SURVIVAL PERIOD AFTER DIAGNOSIS (WEEKS)
2	1B	56		8	Liver enl., med. glands in X-Ray.		4
3	1A	36	oat	20	Liver enl., hoarse voice, pain in spine.	b'opy	5
4	1B	55		28	Liver enl., chest pain, celebral symptoms.		3
5	F11	61		20	Pleural effusion, med. glands in X-Ray, irregular pulse.		8
7	F11	73		12	Pleural effusion.		1
13	1A	56	sq.	>2 yrs.	Med. glands at opn.	op'n.	84
17	1A	58	sq.	3	Med. and paratracheal glands at opn.	op'n.	30
19	FC11	76		4	Pleural effusion, glands left supraclavicular and axillae.		18
21	1A	58		33	Mediastinal glands at p.m.	p.m.	9
25	1A	62	sq.	25	Liver enlarged, emaciated, dysphagia.	p.m.	4
33	F1B	62		8	Liver enlarged, chest pain, mediastinal glands on X-Ray.		21
36	11	65		>2 yrs.	Liver enlarged, pleural effusion, glands in axilla, auricular fibvillation.		52
38	1A	58		6	Liver enlarged, backache, emaciated, paralysed cupola, med. gland on X-Ray.	p.m.	2
40	1A	54	Undiff.	8	Liver enlarged, carina widened, mediastinal glands on X-Ray.	b'opy	12
43	1B	63		>2 yrs.	Liver enlarged, backache.		6
45	FC11	77		1	Liver enlarged, oedema.		1
48	1B	62		11	Pains, gland left supra-clavicular, hoarseness, paralysed left cupola, mediastinal glands on X-Ray.	b'opy	13
54	1A	54	sq.	>2 yrs.	Mediastinal glands at operation.	op'n.	alive
57	11	75		62	Liver enlarged, oedema, auricular fibrillation.		2
60	1A	55		4	Secondaries in liver and spine.	p.m.	5
61	1A	58		38	Peripheral neuritis, secondaries in neck glands.	p.m.	1

TABLE 18a. - Cases with signs and symptoms presumptive of metastases on first diagnosis.

CASE NO.	CLASS	AGE	HIST.	DURATION OF SYMPTOMS BEFORE DIAG. (WEEKS)	EVIDENCE OF METASTASES	DIAG. CON-FIRMED BY	SURVIVAL PERIOD AFTER DIAGNOSIS (WEEKS)
64	11	69		13	Pleural effusion, liver enlarged.		4
70	11	76		13	Pleural effusion, oedema, emaciated.		1
72	11	54		4	Secondary in left radius.		3
73	1B	60		12	Chest pain, emaciated, oedema, dysphagia, backache.		7
84	1B	59		≯2 yrs.	Anorexia, chest pains, carina grossly widened, mediastinal glands on X-Ray.	b'opy	10
86	11			12	Liver enlarged, great thirst, dysphagia, secondary in clavicle.		8
89	1A	63		16	Liver enlarged, skin nodule, secondaries in suprarenals and kidneys.	p.m.	12
91	1A	54	sq.	≯2 yrs.	Secondaries in liver, left clavicle.	p.m.	8
93	1A	68	sq.	≯2 yrs.	Mediastinal glands at operation.	op'n.	32
99	1A	48	sq.	25	Carina widened, paralysed cupola.	b'opy.	32
100	11	80		52	Liver enlarged, pleural effusion, emaciated.		7
101	1A	69	sq.	5	Liver enlarged, paralysed cupola, backache.	b'opy.	12
102	1A	46	undiff.	≯2 yrs.	Mediastinal glands at operation.	op'n.	15
106	1A	47	sq.	38	Pleural effusion, dysphagia, hoarseness, backache.	b'opy.	5
110	1A	60	undiff.	28	Secondaries in glands and liver.	p.m.	1
112	1B	60		≯2 yrs.	Pleural effusion, hoarseness, carina broadened.	b'opy.	14
114	1A	67		≯2 yrs.	Secondaries in liver and spleen.	p.m.	1
115	1A	61		26	Great thirst, secondaries in suprarenals, liver and spleen.	p.m.	1
117	F1A	62	sq.	≯2 yrs.	Enlarged liver, emaciation.	b'copy	8
118	11	46		9	Enlarged liver, dysphagia, hoarseness, backache.		9

TABLE 18a. (Contd). -

CASE NO.	CLASS	AGE	HIST.	DURATION OF SYMPTOMS BEFORE DIAG. (WEEKS)	EVIDENCE OF METASTASES	DIAG. CON-FIRMED BY	SURVIVAL PERIOD AFTER DIAGNOSIS (WEEKS)
123	1A	45		13	Hoarseness, anorexia, large mediastinal and paratracheal glands on X-Ray.		10
126	1A	67		>2 yrs.	Secondaries in spine and liver	p.m.	10
129	1B	64		50	Supraclavicular gland, anorexia, chest pain, oedema.		43
130	1B	73		12	Liver enlarged, hoarseness, dysphagia.		8
133	1B	63		13	Supraclavicular glands, chest pain.		3
134	1A	55		>2 yrs.	Secondaries in liver, back-ache.	p.m.	5
150	1A	52		7	Neck gland, paralysed left cupola, pleural effusion, hoarseness.		6
157	11	73		3	Liver enlarged, oedema.		3
158	11	64		>2 yrs.	Supraclavicular gland, back-ache, oedema, mediastinal glands on X-Ray.		1
162	F1A	48		30	Supraclavicular glands, intercostal swelling.	b'opy.	alive
165	1A	58	Undiff.	34	Pleural effusion, pain, mediastinal glands on X-Ray.	b'opy.	6
173	11	64		37	Paralysed cupola, hoarse-ness, dysphagia.		2
174	11	82		3	Liver enlarged, anorexia, oedema, chest pain.		4
177	11	65		13	Horner's syndrome, vena caval obstruction, paraesthesiae.		1
178	1B	62		50	Supraclavicular gland, carina broadened, oedema, pain in chest.	b'opy.	7
180	1A	60		13	Headache, papilloedema, hemiplegia.	b'opy.	5
181	F1A	62	Undiff.	24	Pleural effusion, carina broadened, pain in chest, vomiting.	b'opy.	12

TABLE 18a (Contd).

CASE NO.	CLASS	AGE	HIST.	DURATION OF SYMPTOMS BEFORE DIAG. (WEEKS)	EVIDENCE OF METASTASES	DIAG. CONFIRMED BY	SURVIVAL PERIOD AFTER DIAGNOSIS (WEEKS)
182	1A	72		3	Pleural effusion, liver enlarged, pericarditis, chest pain.		2
183	11	72		26	Paralysed cupola, pains in chest and abdomen.		2
184	1B	61		9	Liver enlarged, jaundice, mediastinal glands on X-Ray.		8
186	11	61		24	Leucoerythroblastic anaemia due to ? secondaries in marrow		22
187	11	71		24	Liver enlarged, vena caval obstruction, vomiting, backache, pains in chest.	b'opy.	13
191	1A	47	Undiff.	20	Supraclavicular gland.	biopsy	22
193	1A	43	Undiff.	13	Pleural effusion, lysphagia, para aortic glands.	b'opy and oesophagoscopy.	7
195	1A	36	sq.	?2 yrs.	Gland in axilla, pain, infiltrating rib.	b'opy.	40
197	1B	69		8	Liver enlarged, anorexia, pains in chest, emaciation, mediastinal glands on X-Ray.		20
199	1A	50	sq.	30	Thoracotomy showed extensive mediastinal deposits	thoracotomy	27
200	11	57		?2 yrs.	Gland in axilla, subcutaneous deposits, vena caval obstruction, mental confusion.		1
203	11	56		?2 yrs.	Hemiplegia, mediastinal glands on X-Ray.	b'opy.	5
205	F1A	48	Undiff.	22	Pleural effusion, liver enlarged, intercostal lump, enlarged glands on X-Ray.	biopsy	43
206	1B	64		50	Liver enlarged, jaundice, vena caval obstruction, anorexia, dysphagia, paralysed left cupola.		17
207	F11	65		52	Paralysed cupola, oedema, chest pain.		9
208	11	71		71	Vena caval obstruction, pain.		1

TABLE 18a (Contd.)

CASE NO.	CLASS	AGE	HIST.	DURATION OF SYMPTOMS BEFORE DIAG. (WEEKS)	EVIDENCE OF METASTASES	DIAG. CON-FIRMED BY	SURVIVAL PERIOD AFTER DIAGNOSIS (WEEKS)
209	1A	48		>2 yrs.	Liver enlarged, pleural effusion, skin nodule, dysphagia, irregular pulse, emaciation.	b'opy.	10
211	11	62		>2 yrs.	Supraclavicular gland, liver enlarged.	biopsy	2
222	1A	64	Undiff.	40	Pleural effusion, paralysed cupola, carina widened.	b'opy.	20
223	1A	60	sq.	28	Paralysed left cupola, chest pain, sickness, mediastinal glands on X-Ray.	b'opy.	17
224	F11	74		21	Pleural effusion, sciatic pains.		4
225	1A	60	sq.	26	Carina widened, mediastinal glands on X-Ray, chest pain.	b'opy.	9
228	1B	76		17	Mediastinal glands on X-Ray, intercostal pain.		42
231	F1B	72		70	Neck gland, paralysed cupola, pain, mediastinal glands on X-Ray.		8
234	11	70		26	Supraclavicular glands, liver enlarged, pleural effusion, chest pain.		1
235	F1B	50		30	Infraclavicular gland, paralysed cupola, liver enlarged, vena caval obstruction.		7
239	F1A	56	Adeno	9	Mediastinal glands at operation.	op'n	38
240	11	70		36	Paralysed cupola, hoarseness, right pupil small, mediastinal glands on X-Ray.	b'opy.	36
241	1A	53	Undiff.	16	Liver enlarged, anorexia, emaciated, mediastinal glands on X-Ray, diarrhoea, pains in chest.	b'opy.	9
244	F11	66		>2 yrs.	Pleural effusion, chest pains, fibrillating.		2

TABLE 18a. (Contd.) - Total = 88 cases (2 alive).
Average survival period of 86 cases = 12 weeks.

CASE NO.	CLASS	AGE	HIST.	DURATION OF SYMPTOMS BEFORE DIAG. (WEEKS)	SIGNS & SYMPTOMS OF METASTASES	DIAG. CON-FIRMED BY	SURVIVAL PERIOD AFTER DIAGNOSIS (WEEKS)
6	1A	59	sq.	12	Oedema. Med. gl. in X-Ray.	b'opy.	15
30	1A	55	sq.	33	Pain. Med. gl. in X-Ray.	b'opy.	25
77	1A	57		8	Pain. Med. gl. in X-Ray.	p.m.	27
107	1A	60		26	Pain. Med. gl. in X-Ray.	b'opy	17
116	F1A	64	Undiff.	27	Pain, anorexia, vomiting, emaciated.	b'opy.	9
151	1B	67		>2 yrs.	Haemoturia. Abd. pain, Med. gl. in X-Ray.		4
166	1A	68		>2 yrs.	Emaciated, dysphagia, sup. med, obstruction, med. gl. on X-Ray.	b'opy.	24
167	1B	65		>2 yrs.	Emaciated. Pain in back, hoarse.	l'opy.	11
189	1A	69	Undiff.	13	Dysphagia. Vena cavae obstruction.	b'opy.	23
201	11	73		14	Oedema. ? pl. eff. anorexia.		11
212	11	70		12	Emaciated, Med. gl. in X-Ray.		2
226	11	72		8	Pain, oedema, anorexia.		1
227	1A	43	Undiff.	14	Hoarse, Broadening carina	b'opy.	39
242	11	82		25	Liver end. Med. gl. in X-Ray.		17

Total = 14 cases (none alive);

Average survival of 14 cases = 16 wks.

TABLE 18b. - Cases with signs and symptoms presumptive of metastases after initial investigation.

CASE NO.	CLASS	AGE	HIST.	DURATION OF SYMPTOMS BEFORE DIAG. (WEEKS)	REMARKS	DIAGNOSED CONFIRMED BY	SURVIVAL PERIOD AFTER DIAG. (WEEKS)
1	$\overline{11}$	55		16	Refused operation.		99
12	1A	53	sq.	2 yrs. +	Refused op.	b'opy.	104
20	1A	60	Adeno	14	Aur. Fib. Some pain.	b'opy.	52
23	1A	72	Sq.	12	Aet. 72.	b'opy.	93
51	1A	60	sq.	5	B.P. 200/100 Refused op.	b'opy.	64
94	11	65		0	M.M.R. Refused op.		Alive
96	1A	60	sq.	2 yrs. +	Ch. Bronchitis. Growth very near carina.	b'opy.	31
109	F1A	59	Undiff.	22	Ankylosing spondylitis	sputum	30
127	1A	52	Adeno	26	Operated on.	op.	Alive
128	1A	59	sq.	6	Operated on.	op.	Alive
131	1A	51	Undiff.	39	Operated on.	op.	87
138	F1A	80	sq.	2 yrs. +	Age 80	p.m.	60
145	1A	46	sq.	8	Operated on.	op.	Alive
146	1B	60		2 yrs. +	Silicosis & ch. br. & emphysema.		Alive
147	1A	64	sq.	6	Unfit opn - aortic incompetence.		46
161	11	58		2 yrs. +	Hypertension, poor g/c.	b'opy.	65
172	1A	76	Adeno	34	Age 76		46
221	1A	60	sq.	2 yrs. +	Operated on.	op.	14
243	1A	78		2 yrs. +	Age 78. Diagnosis in doubt in site of p.m.	p.m.	5
264	1A	52	Adeno.	52	Operated on.	op.	Alive

Total = 20 cases (6 alive)

Average survival of 14 cases = 54 weeks

TABLE 18c. - Cases free from metastases on first diagnosis.

CASE NO.	CLASS	AGE	HIST.	DURATION OF SYMPTOMS BEFORE DIAG. (WEEKS)	EFFUSION	DIAG. CON-FIRMED BY	SURVIVAL PERIOD AFTER DIAGNOSIS (WEEKS)
154	1A	51	sq.	2 yrs. +	Yes.	Operation	Patient Still Alive

AND FOUR CASES INCLUDED IN TABLE 18a. (7, 70, 186, and 244).

TABLE 18d. - Cases with effusion on first diagnosis but no other evidence of metastases.

Table 18 is summarised in Table 19. This shows that in my opinion approximately 71% to 83% of cases have metastases on first diagnosis.

This may seem a high figure. Rosenblatt and Lisa (1956), give 42%, Oswald (1956) found at the time of diagnosis that 26% of cases had involvement of extra thoracic structures and another 23% to have obvious spread to the mediastinum. Bignall (1955), found, out of 317 cases, that thoracotomy was precluded in 41% of cases because of intra thoracic or extra thoracic spread, and that in another 7% of the total, resection was impossible after thoracotomy.

As will be seen from Table 18, 41 or 33% of my cases were dead within six weeks of diagnosis. Most of these cases would not be referred to special clinics or surgical centres, and they are quite numerous enough to account for the difference between my figures (which include all the cases occurring in one area), and those in series of cases already partially selected for surgery.

GROUP	NO. OF CASES	% OF TOTAL
Cases with strong evidence of metastases on first diagnosis.	88	71%
Cases with presumptive evidence of metastases after initial investigation.	14	12%
Cases with effusion on first diagnosis but no other evidence of metastases.	1	1%
Cases free from metastases and effusion on first diagnosis.	20	16%
TOTAL	123	100%

TABLE 19. - Evidence of metastases on first diagnosis in 123 cases of bronchial carcinoma.

The figure of 70% to 80% of cases with metastases at first diagnosis includes of course those operated on and found to have spread to mediastinal glands. These amounted to 6 cases, about 5% of the total.

Table 18d postulates 20 cases free from metastases out of the total 123. Of these 5 were operated on leaving 14. In Table 12, Chapter 6, these fourteen are seen to be made up of 4 refusing surgery, 5 rejected by the physicians because of heart disease or other conditions and 5 either too old for operation or rejected by the surgeon after assessment.

It is possible to look at this problem in another way.

Metastases as the cause of the very first and major single presenting symptom or sign occurred in 35 cases, as follows:-

Abdominal pain	12 cases	
Palpable glands	8 cases	
Secondary in bones	5 cases	(clavicle 3)
Backache	5 cases	
Superficial intercostal Swelling	4 cases	
Cerebral symptoms	3 cases	
Leucoerythroblastic anaemia	1 case.	

In an additional 29 cases the very first major symptom was suggestive of the presence of metastases. These were as follows:-

Dysphagia	9 cases
Pleural effusion	7 cases
Hoarse voice	6 cases
Vena caval obstruction	5 cases
Peripheral neuritis	1 case
Excessive thirst	1 case

This indicates the possibility that in more than 50% of cases the first symptom that the patient noticed and which made him go to his doctor was due to a metastasis. This suggests the existence of a not inconsiderable silent period. (See Chapter 15).

The number presenting with abdominal symptoms may seem high. There were 12 such cases of whom 6 were admitted direct to surgical wards.

The percentage of metastases to abdominal sites is however perhaps higher than is generally realised. Rosenblatt and Lisa (1956g) giving the site of metastases in 208 antopsies found abdominal lesions as follows:- Liver 71, adrenal 54, kidney 37, spleen 15, pancreas 7, abdominal glands 56, peritoneum 8, omentum 1, small bowel 4 and large bowel 1.

The relative frequency of these compared with other metastases will be seen from Table 20.

Of my 12 cases presenting with abdominal symptoms only 5 were comfirmed histo-pathologically. It seems possible as suggested in Chapter 3, Section D that suspected symptoms in the abdomen could in fact be due to an undiscovered primary with secondary lesions in the lungs. This problem was ~~also~~ discussed in Chapter 7.

Four cases presented with superficial swellings (162, 195, 205, 235). In each case the site was the right pectoral area.

FREQUENCY	SITE	NO. OF CASES
1	Tracheo-bronchial glands	167 167
2	* Liver	71
3	Mediastinal glands	57
4	* Abdominal glands	56
5	* Adrenals	54
6	* Kidney	37
7	Ribs	35
8	Cervical glands	27
9	Vertebrae	25
10	Pericardium	23
11	Brain	21
12	* Spleen	15
13	Myocardium	13
14	Axillary glands	12
15	Muscles	10
16	Dura	9
17	* Peritoneum	8
18	* Pelvis	8
19	* Pancreas	7
20	Skin and subcutaneous	5
21	* Small bowel	4
22	Skull	4
23	* Pelvic glands	4
24	Unspecified bones	3
25	Sternum	3
26	Inguinal glands	1
27	Clavicle	1
28	Femur	1
29	Humerus	1
30	Spinal cord	1
31	* Large bowel	1
32	Diffuse bone marrow	1

(* Abdominal sites).

TABLE 20. - Sites of metastases in 208 autopsies on bronchial carcinoma cases. (After Rosen-Blatt & Lisa, 1956g).

Three were women. In all four cases the X-Ray appearance was of a dense hilar mass, at the right root in 3 cases and at the left root in one. Inno case was the histology determined for certain. In all four cases X-Ray therapy was given which caused regression of the superficial lesion.

Two cases (60, 154) had haematuria associated with the presenting symptoms, but the period of survival was only a month in each case. A third case (91) had haematuria as a terminal symptom. At necropsy a secondary deposit was found in the left kidney. As will be seen from Table 20, Rosenblatt and Lisa list the kidney as the sixth commonest metastatic site.

One case of leucoerythroblastic anaemia was met with (186) presumably due to multiple secondary deposits in the bone marrow as mentioned in Table 20. This case, unfortunately, was not confirmed histologically; it has been described in Chapter 4 P. 48.

The second factor connected with symptoms and signs that interests me from the epidemiological aspect is their duration before a diagnosis is made.

This period is an approximation only, because, while in most cases there is a fairly definite date of onset of symptoms, there is a group of cases with symptoms of long and indeterminate duration. In the various estimates of duration of symptoms already given, for examples Tables 4, 6, 10, 14, 18, an approximate estimate for this group of cases has had to be used.

Table 21 shows that there were 31 such cases (25%) with a history of symptoms for over two years before the carcinoma was diagnosed. All these were under periodic treatment for chronic bronchitis, emphysema, tuberculosis, pulmonary fibrosis, etc. for periods up to 35 years before the diagnosis of carcinoma was made. In most of these cases the long standing symptoms merged imperceptibly into those manifestly due to the carcinoma.

It will be seen from Table 18 that 24% (33) of the total cases gave a duration of symptoms of less than three months, 24% (33) of between three and six months, 12% (16) of between six and nine months and 5% (7) between nine and twelve months. There ~~are~~ were only 2 cases with a history of more than one year but less than two years.

In contrast 24% (32) gave a history of over two years. Perhaps this suggests that in these cases the cause of the long standing symptoms was not the carcinoma, which probably supervened on a simple chronic condition.

In Table 21 an attempt has been made to give the minimum duration of symptoms in these 32 cases definitely related to the carcinoma, and this works out at an average of only six months. Yet as previously stated the change from the long term to the short term symptoms in most of the cases listed in Table 21 was so gradual as to be imperceptible and I feel that in some cases the period of symptoms due to the carcinoma may be longer than we think.

CASE NO.	PREVIOUS TREATMENT BEFORE DIAGNOSIS				DIAGNOSIS AT THAT TIME	ESTIMATED DURATION OF SYMPTOMS DUE TO BR. CA. BEFORE DIAGNOSIS.		Histology	Operated on	Survival after diagnosis (weeks)
	by	for	by	for		MAX.	MIN.			
154	G.P.	35 yrs.	Chest C.	11 yrs.	? T.B.	35 yrs.	2 yrs.×	sq.	yes	alive
151	"	30 yrs.			Bronchitis	30 yrs.	7 mos.			4
126	"	30 yrs.			bronchitis	30 yrs.	2 mos.			10
138	"	30 yrs.			b'ectasis	30 yrs.	8 mos.	sq.		60
167	"	25 yrs.			bronchitis	25 yrs.	3 mos.			11
161	"	20 yrs.			bronchitis	20 yrs.	9 mos.			65
96	"	20 yrs.			bronchitis	20 yrs.	1 yr.	sq.		31
166	"	20 yrs.			bronchitis	20 yrs.	3 mos.			24
211	"	20 yrs.			bronchitis	20 yrs.	5 mos.	ana.		2
158	"	20 yrs.			asthma	20 yrs.	4 mos.			1
112	"	20 yrs.			bronchitis	20 yrs.	3 mos.			14
54	"	17 yrs.	Chest C.	3½ yrs.	bronchitis	17 yrs.	3 mos.	sq.	yes	alive
200	"	15 yrs.			bronchitis	15 yrs.	6 mos.			1
203	"	15 yrs.			bronchitis	15 yrs.	5 mos.			5
146	"	12 yrs.			bronchitis	12 yrs.	6 mos.			alive
195	"	11 yrs.	Chest C.	10 yrs.	Palm fibros.	11 yrs.	7 mos.×			40
43	"	10 yrs.			bronchitis	10 yrs.	4 mos.			6
84	"	10 yrs.	M.O.P.D.	4 mos.	bronchitis	10 yrs.	3 mos.			10
93	"	10 yrs.	M.O.P.D.	1 yr.	bronchitis	10 yrs.	4 mos.	sq.	yes	32
117	"	10 yrs.			bronchitis	10 yrs.	4 mos.	sq.		8
209	"	9 yrs.	M.O.P.D.	8 mos.	bronchitis	9 yrs.	6 mos.×			10
36	"	8 yrs.			bronchitis	8 yrs.	4 mos.	~~sq.~~		52
91	"	8 yrs.	Chest C.	6 yrs.	giant cyst	8 yrs.	4 mos.×	ana. ~~sq.~~	~~yes~~	8
221	"	8 yrs.			pleurisy	8 yrs.	8 mos.	sq.	yes	14
13	"	7 yrs.	M.O.P.D.	4 mos.	palm fibros.	7 yrs.	4 mos.	sq.	yes	84
243	"	6 yrs.			bronchitis	6 yrs.	2 mos.			5
244	"	5 yrs.	M.O.P.D.	5 yrs.	asthma	5 yrs.	5 mos.			2
114	"	4 yrs.			bronchitis	4 yrs.	4 mos.			1
134	"	4 yrs.			angina p.	4 yrs.	2 mos.			5
12	"	3 yrs.	M.O.P.D.	15 mos.	bronchitis	3 yrs.	18 mos.×	sq.		104
102	"	3 yrs.	Chest C.	2 yrs.	palm fibros.	2 yrs.	2 mos.	ana.	yes	15
					Average:	14 yrs.	6 mos.			

TABLE 21. - Cases with a history of continuous chest symptoms for 2 years or more.

× = delay in diagnosis.

Two such cases are described in detail. One of these (Westwell-54), Chapter 3, Fig. 3, gave a history of about three years before diagnosis. The other (Ashton-154), Chapter 11, Fig. 9, gave a fairly definite history of five years before diagnosis.

The overall average period of symptoms before diagnosis for the 123 cases may be estimated at approximately 31 weeks - i.e. 7 months. Oswald (1956) found the average duration of symptoms prior to diagnosis was $3\frac{1}{2}$ months. This seems a low figure. Nicholson et. al. (1957) found their cases gave a pertinent history of six months. Bignall (1955) stresses the difficulty of giving a reliable average figure, because the possible maximum and minimum periods vary widely in many cases.

The average period of symptoms before diagnosis may vary with the histological type, as shown in Table 14, but very little difference in the extent of the disease at the time of diagnosis could be detected between the 16 confirmed cases with the longest period of symptoms(all over 2 years), when compared with the 16 confirmed cases with the shortest period of symptoms (seven weeks or less).

In each group 5 were operated on with about equal results, the survival period of the 11 non-operated in each group was exactly equal (19 weeks). There was no difference in the prima facie extent of the X-Ray changes or in the histology. In the long-history group this was known in 8 cases (six squamous and two undifferentiated), in the short-history group it was known in six (four squamous

and two undifferentiated). There was a slight difference in the sumptoms: dyspnoea, cough, sputum, clubbing, loss of weight and abdominal symptoms being slightly more in evidence in the long-history group.

There is a serious source of bias attached to the duration of symptoms among the old and poor cases who had neglected themselves for an indefinite period and had been admitted more or less as emergencies to hospitals in a pre-terminal state. A good number of these were too ill on admission to give an accurate history, or died before I could interview them. In many cases the patient had not eaten anything for two weeks, or he had severe vena caval obstruction, heart failure, oedema, abdominal distension, hoarseness, emaciation, pain etc. In such cases the emphasis was on the immediate care and alleviation of symptoms. The history and the duration of the initial symptoms tended to be lost sight of.

CHAPTER 10

X-RAY FINDINGS

In this series of 123 cases of bronchial carcinoma there were eight who had not had a chest X-Ray. One of these was ~~for~~ confirmed histo-pathologically. The other seven are discussed in Chapter 4.

Four other cases also discussed in Chapter 4 showed pleural effusion only.

The epidemiological significance of the X-Ray picture includes any help it may give us as to the stage to which the disease has progressed.

Unfortunately the amount of the X-Ray changes, like the duration of symptoms, is not always in direct proportion to the extent of the disease.

Mitchell (1955), described four cases with clear X-Rays confirmed by bronchoscopy, only one of which was operable.

In this series there were three cases with more or less normal chest X-Rays, but unfortunately ~~more~~ they were not verified histo-pathologically.

As stated in Chapter 6 considerable importance is attached to the possibility of detecting hilar glands in lateral X-Rays.

Of the 6 cases found to have malignant glands at operation what was thought to be glands was seen on all the six X-Rays. Admittedly in one out of the other seven operated cases non-malignant glands were seen.

In all 7 cases where widening of the carina was specially mentioned at bronchoscopy, glands were seen in the lateral X-Rays.

In many cases however it was not possible to decide whether the shadow seen ~~is~~ was due to glands or to the tumour itself. Thus, Walter and Pryce (1955c), found among resected specimens, 47% of the cancers to arise from nominate bronchi. Rosenblatt and Lisa (1956d), found a much higher percentage of cancers arising from the main and lobar bronchi among necropsy cases, than they did among resected cases.

It is often difficult to differentiate between the X-Ray appearance of glands and of collapsed segments.

Bishop (1957), advocates tomograms in both p-a and semi-oblique positions to determine mediastinal invasion when deciding resectability.

Radiological elevation of the diaphragm with, in most cases, paradoxical respiration was present in 15 cases (12%). In all these cases except one, where no lateral chest X-Ray was available, enlarged mediastinal glands were considered to be able to be made out radiologically. In only 4 cases

was the histology known; in three it was squamous, in one undifferentiated. The average survival period after diagnosis of these 15 cases was 12 weeks.

Among the 131 non-carcinoma cases there were 3 with definite elevation of the diaphragm. One was just drawn up medially as occurs in pulmonary fibrosis. The other 2 had definite paradoxical movement on screening.

In this series of cases the right cupola was paralysed in seven cases and the left in eight.

There were 11 cases complaining of hoarseness on diagnosis or shortly after.

In the X-Ray in every case it was considered that enlarged mediastinal glands could be seen. The carcinoma in 8 cases (48, 106, 112, 134, 150, 173, 209, 237) was on the left side.

In one of the three cases (123) where it was on the right side there were massive upper mediastinal glands visible in the p-a film. In the second case (130) there were heavy shadows in the lateral view and the E.N.T. specialist stated that there was paralysis of the left vocal cord. In the third case (240) the lesion was a dense right hilar mass and there was associated paralysis of the right cupola and the right pupil was smaller than the left although both reacted to light.

The average survival time for these 11 cases was 13 weeks.

The X-Ray picture of the eight cases who complained of dysphagia on diagnosis or shortly after showed lesions on the left side in 5, (106, 126, 193, 206, 209), and on the right side (86, 118, 126) in three. In only three out of the eight cases were mediastinal glands considered to be visable on the X-Ray. The average survival period was 9 weeks.

In this series there were 4 cases discovered by mass radiography. All ~~three~~ four were early cases and 3 were advised operation, The fourth being misdiagnosed. This was refused by one, but in the other two no glands were found and they are now well and working. The case who refused is alive but ill.

In this area the No. 1 M.M.R. Unit of the Manchester Regional Hospital Board finds about 9 cases a year out of 40,000 examinees, (Stalker 1951). This means that in the area covered by the present study, with a population of 250,000 there are an unknown number, perhaps 30 to 50, cases of incipient and maturing bronchial carcinomas already with radiological changes.×

According to Mayer and Maier (1956c), the Boston Community Survey revealed one confirmed case per 13,500 persons, and the Los Angeles Survey one case per 8000 persons.

× Since then the number of cases found by M.M.R. has increased, but the extent of the increase cannot easily be assessed because:
a. Prior to 1955 bronchial carcinoma was not listed separately but was included in the group "intrathoracic new growths" which contained benign and metastatic lesions.
b. Mass radiography statistics are not adjusted for changes in diagnosis after 4 to 6 months.

Brett et al, (1956) with a static M.M.R. Unit at Islington found 1 case per 750 examinees. The type of population group dealt with by M.M.R. of course varies widely.

Unfortunately, repeated X-Rays of the same individual at very short intervals even three monthly, would not necessarily ensure that any lesion would be found in an operable state. This would further increase the cost of discovery by mass radiography, put by Cohn (1956) at 10,000 dollars and by Mayer and Maier (1956d), at 5000 dollars.

Overholt operating on 35 cases discovered by M.M.R. found 75% free from lymphatic spread.

Cohn (1956), however states that when half the population of San Diego were X-Rayed by M.M.R., of 20 cases of bronchial carcinoma found, none were free from symptoms and a follow-up showed an average length of life of 9 months.

From the point of view of the prognosis in the individual case however, and also of the surgeon's results the value of mass radiography can hardly be overemphasised.

As stated in Chapter 7, it is very difficult even at post-mortem to decide on the point of origin of a bronchial carcinoma; the X-Ray appearances are, in this respect, even more difficult to interpret.

It is possible, however, to classify X-Ray appearance quite simply into seven main groups:- coin shadows, linear streaking or pneumonitis, segmental collapse, dense hilar

shadows, lobar or massive collapse, abscesses, and effusions.

This has been done in Table 22 for all the cases (81 in number), where the diagnosis is beyond all ambiguity, the X-Rays fully available, and the history known in reasonable detail.

GROUP	X-RAY APPEARANCE						
	Coin shadow	Linear streaking or pneumonitis	Segmental collapse	Dense hilar shadow	Lobar or massive collapse	Abscess	Effusion only
Total no. of cases	2	17	14	26	19	2	1
Av. duration of symptoms before diagnosis: weeks	39	34	33	29	38	71	38
Operated	2	3	4	3	0	1	0
Op. and found free from glands	2	2	2	1	0	0	0
Op. 2 yr. survivors	2	1	1	1	0	1	0
Non-operated	0	14	10	23	19	1	1
Non-op. 2 yr. survivors	0	0	0	0	2	0	0
Survival-weeks							
Total deceased	0	40	17	16	14	11	5
Op. "	0	80	20	34	0	0	0
Non-op. "	0	34	17	16	14	11	5
Cases with Known histology:-							
Total	2	12	9	9	9	1	1
Sq.	0	9	7	6	4	1	1
Undiff.	0	2	2	2	4	0	0
Adeno.	2	1	0	1	1	0	0
Prognosis	poor	bad	v. bad	v.v.bad	v.v.v. bad		

TABLE 22. - Eighty-one confirmed cases classified according to the appearance of the first X-Ray.

Table 22 suggests that coin shadows have the best prognosis, especially those discovered by M.M.R. as the two in this series were. Even then they gave on careful questioning a history of about 39 weeks.

The survival period seemed to be best among the other groups for those cases showing linear streaking or pneumonitis on the first X-Ray. Cases showing segmental collapse seemed to have a less good survival period although a similar number were of squamous type and about an equal number operable. Cases showing dense hilar shadowing seemed to be less suitable as operation starters. None of the 19 cases with dense lobar or massive collapse were operable. They gave quite a long history but no longer than the two cases with coin shadows that had been picked up by M.M.R.

Perhaps the 19 cases contained more undifferentiated types and/or were faster growing. The other possibilities are that they were even more symptomless than the M.M.R. cases in the early stages, or else the periods of symptoms as stated are wrong.

CHAPTER 11

PLEURAL EFFUSIONS

In 19 cases a pleural effusion was present on first diagnosis.

None of these cases, 4 male and 5 female, were of the CII type with a possible doubt as to the certainty of the diagnosis.

The high proportion of female cases, 8 out of the total 19 further suggests a possible doubt as to the etiology.

The 19 cases include the four cases of ? pure heart disease mentioned in Chapter 4, (7, 70, 186 and 244). These cases survived on average only six weeks so the effusion has been regarded as a manifestation of secondary spread and they have been included in Table 18 a in spite of the diagnostic doubt.

Six of the 19 effusion cases gave definite cardiac symptoms ; pystolic murmur plus high blood pressure 2 cases, arterio-sclerosis 1 case, fibrillation 2 cases and heart block one case.

The average age for males and females was 61 and 63 years, the same as for all the male and female cases.

The average duration of symptoms before diagnosis for the female cases was 24 weeks compared with 36 weeks for all female cases. The average duration of symptoms for the male

cases was 46 weeks compared with 31.5 weeks for all male cases.

All the cases with one exception were considered to have evidence of metastases on first diagnosis. Eighteen of the nineteen cases are now dead, the survival period for both males and females from diagnosis being only 12 weeks, compared with a survival period for all deceased cases of 17 weeks.

Only one case was operated on, namely the survivor mentioned above, (Ashton - 154), illustrated in Fig. 9.

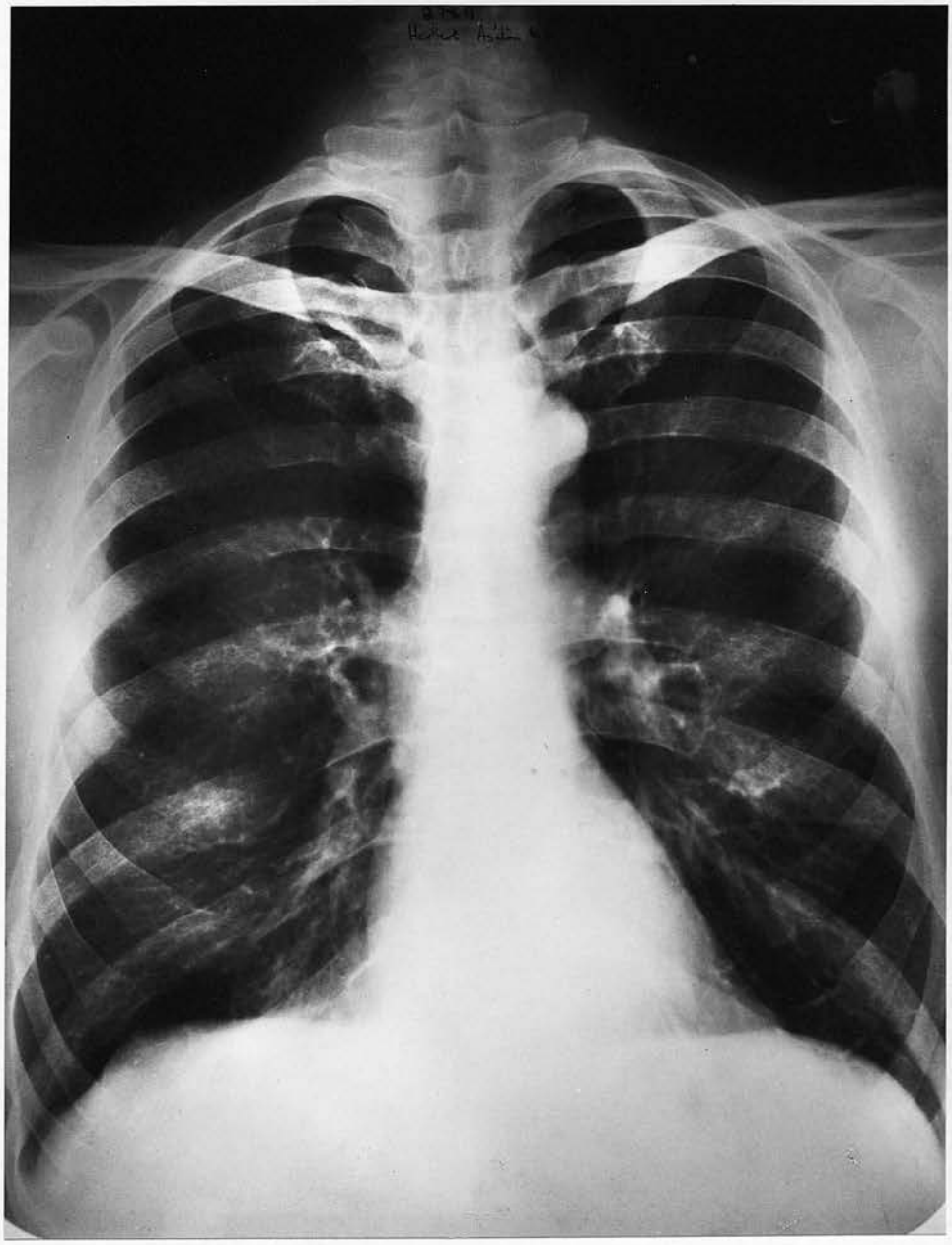


FIG. 9a. - Carcinoma with long history and a large pleural effusion successfully operated on.

Patient had already been under the Chest Clinic for 6 years with cough and "increased fibrosis left hilar region."

Male, age 51, 28·8·50. (Ashton - 154).

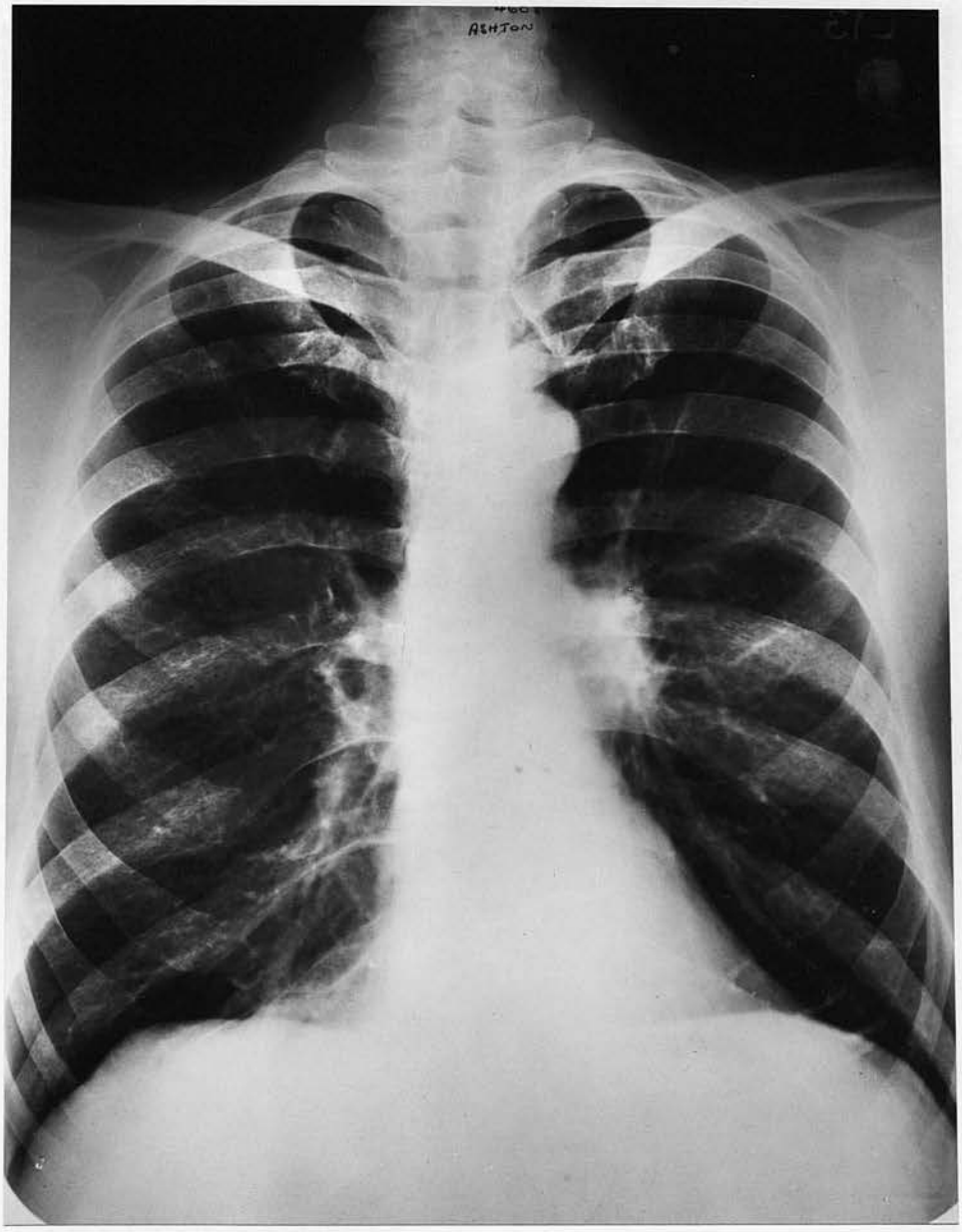


FIG. 9b. - Do. 21·8·53. Hilar shadow bigger. Carcinoma suspected but bronchoscopy negative.

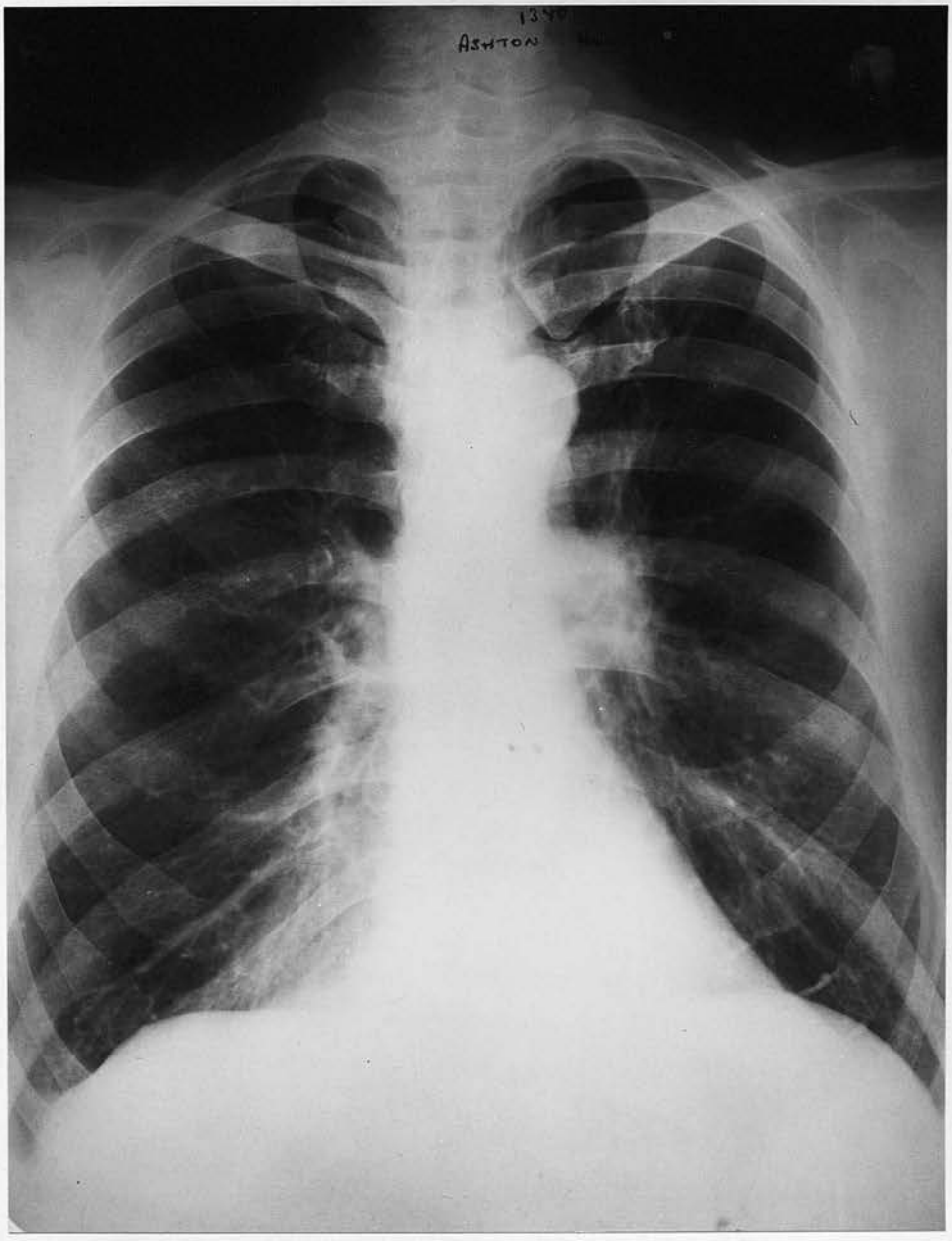


FIG. 9c. - Do. 1·3·54.

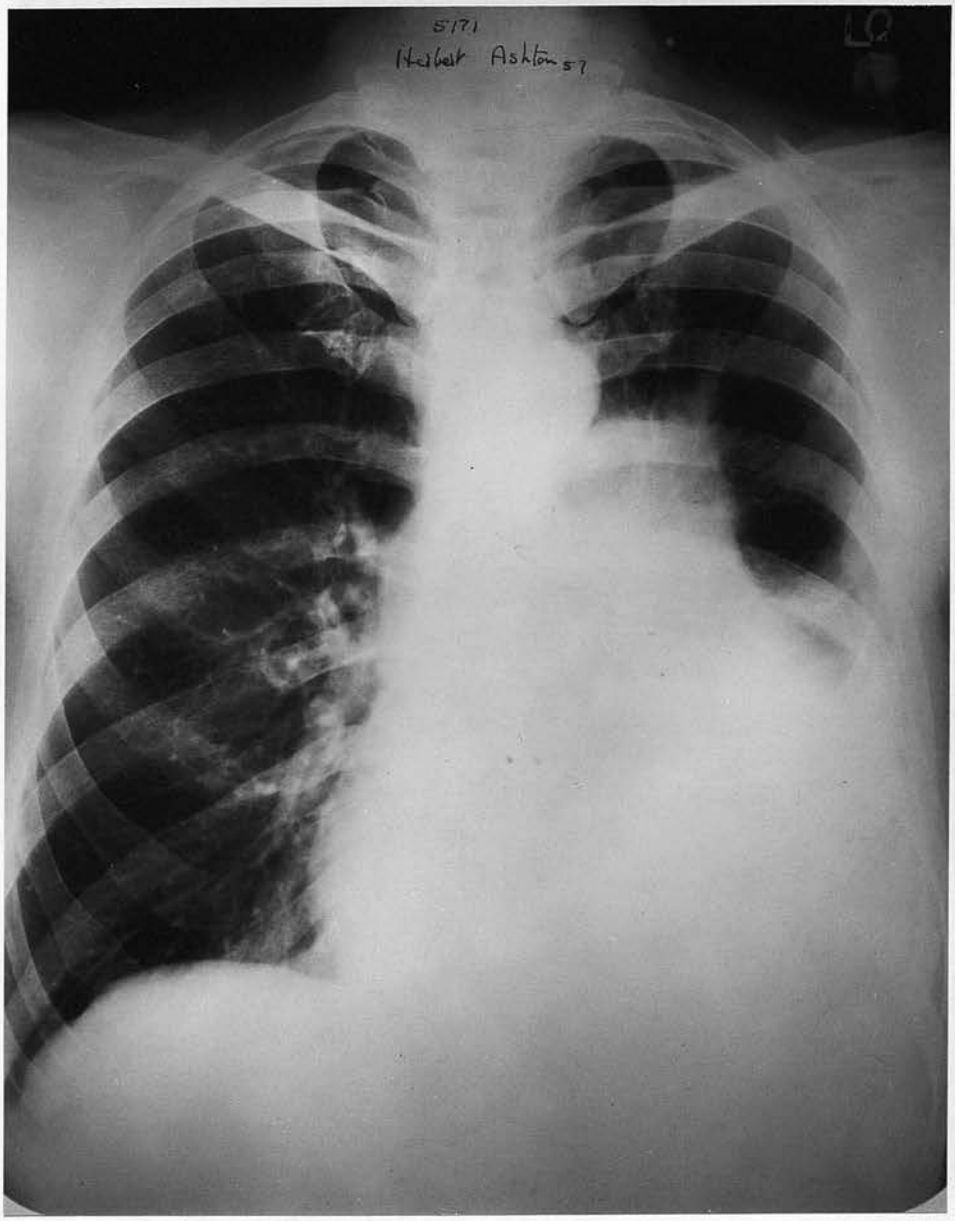


FIG. 9d. - Do. 12·8·55. Blood stained sputum for two years. Large left pleural effusion.

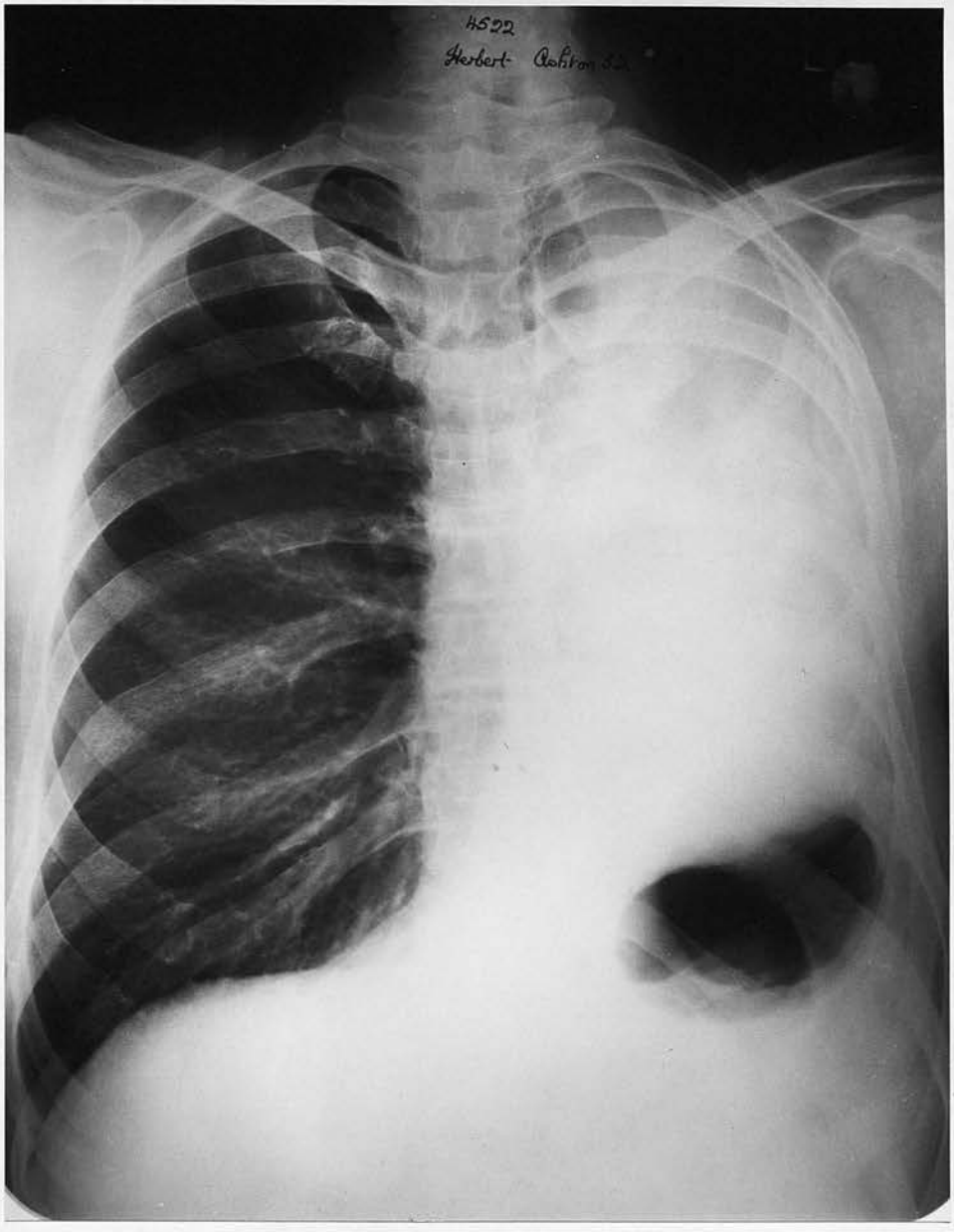


FIG. 9e. - Do. 18·7·56. Patient well and working. At pneumonectomy on 1·9·55 the mediastinal glands had been found free from secondaries.
(The patient is still well and working as at 30·9·57).

He was a man aged 51 who had smoked 25 cigarettes a day all his life. He stated that he was suspected of having tuberculosis in 1921-22, and had always had a cough.

He came under the Chest Clinic again in 1944 with cough, bronchitis and emphysema and shortness of breath. In view of the alleged previous history he was X-Rayed from time to time.

The first available film (Fig. 9a) is dated 28.8.50. when the patient complained of breathlessness and pains in the left chest.

By 1953 he had brought up some blood and the X-Ray (Fig. 9b) showed a suspicious enlargement of the left root. Bronchoscopy however was negative and he kept on working. A film in 1954 (Fig. 9c) showed no change.

By June 1955 he had lost a stone in weight, his spleen was enlarged, he was more breathless and still bringing up purulent sputum and blood.

In August 1955 he was admitted to hospital with a left pleural effusion, (Fig. 9d.) which on aspiration was clear and contained only 4.3 m.g.m.% of protein. The cells were lymphocytes 70%, polymorphs 26% and eosinophils 4%. Bronchoscopy now revealed a growth in the dorsal segment of the left lower lobe and biopsy revealed a well-differentiated non-keratising squamous-celled carcinoma.

Left pneumonectomy was carried out on 1.9.55 and to everybody's surprise no malignant glands were present at operation. However, as part of a general scheme he was given post-operative deep X-Ray therapy.

The patient is now - over two years later - well and working.

This case is interesting for two reasons:-

1. Because a large pleural effusion was present without apparently any secondary spread and without precluding operation.

2. It is one of those cases where a long history of bronchitis appears to merge imperceptibly into carcinoma.

A few such cases have been met with, and a similar case has previously been described (Fig. 3 P. 21). One wonders how long the carcinoma is present in these cases before diagnosis, is it years? This problem will be mentioned again in Chapter 14, P.154, and Chapter 15, P.188.

Pleural effusion associated with bronchial carcinoma may be due to metastatic invasion of the membrane, or to secondary infection distal to the tumour following on sepsis, collapse or infarction. Causation by clogging of lymphatics, or liver damage, or heart failure has also been suggested.

In the case described above it seems unlikely that the tumour had metastasised to the pleura or lymphatics.

In only 7 cases out of the 19 effusions in this series was the histology known. This was squamous in four cases and undifferentiated in three.

The fluid was aspirated in 12 cases. In five cases it was straw-coloured and in four cases blood-stained. In four cases cytology was reported as suggesting malignancy.

The X-Ray pictures on first diagnosis suggested a combination of pleural effusion plus massive collapse in 5 cases. In 6 cases there was a hilar mass plus a small pleural effusion, in two cases a large effusion plus ? collapse, in two cases smaller bilateral effusions plus ? collapse, in one case a moderate effusion and nothing else visible, in one case lower lobe shadowing plus a small effusion, and in one case, unconfirmed histopathologically, what was considered to represent bilateral carcinomatosis plus a small effusion. In addition there was the operated case described above which started radiologically as a slowly enlarging left hilar mass leading to collapse of the left lower lobe and effusion.

In ten cases the effusion was on the left side and in 7 on the right. In two cases there were small effusions at both bases associated with heart failure.

No case of empyema was met with on first diagnosis. Rosenblatt and Lisa (1956h), give a 7% incidence at post-mortem.

There was one case of septic pericarditis (J. J. Smith - 182, Ch. 3, Fig. 5). Rosenblatt and Lisa (1956h), give a 1% incidence of pericarditis and pericardial effusion at post-mortem.

In a large series of necropsy cases with pleural effusion Rosenblatt and Lisa (1956h), found 22% without neoplastic invasion of the pleura.

Hanbury et al (1954), described a 10% incidence of pulmonary infarction in operation specimens, mostly moderately old, showing organisation, but only one with septic changes.

CHAPTER 12

SURVIVAL PERIOD AND PROGNOSIS

I have chosen as the survival period the period between diagnosis and death. The stage in the life history of the disease when diagnosis takes place may of course vary greatly from case to case.

Delay in diagnosis may cause the period of symptoms before diagnosis to be over-estimated and the "survival period" unduly short. Thus Rosenblatt and Lisa (1956i), found a quarter of their hospital first admissions died within 10 days.

I have a good number of such cases where the survival period appears much too short because of delayed diagnosis. However there seems to be no practical alternative way of estimating this period.

Table 23 shows the actual persons surviving by 30.9.57 out of the 123 cases of bronchial carcinoma diagnosed during 1955. There were no survivors of an undifferentiated lesion, and of the three non-operated survivors none had been verified histologically, although one of these, a female case, was queried as either an adenoma or an adenocarcinoma at bronchoscopy biopsy.

Case No.	oper-ation	Deep X-Ray	Sex	Age	Histology	Evidence of metastases on first diag. Remarks	Med. glands at operation	Dur. of symp. before diag. (weeks)	Sur. after diag. (weeks)	Present Con.
44	no	no	M	65	not known	no, M.M.R. pick up, coin shadow operation refused.	n/a	nil	120	still working
46	no	no	M	60	not known	no, bronchitis and emphysema	n/a	2 yrs +	116	v. ill
62	no	yes	F	48	? adeno-carcin.	yes, intercostal swelling. Glands rt. supra-clav.	n/a	30	111	v. ill
54	yes	no	M	54	sq.	yes	yes	2 yrs +	133	v. ill
27	yes	no	M	52	adeno-carcin.	no. M.M.R. pickup	no	26	124	well & working
28	yes	no	M	59	sq.	no. M.M.R. pickup	no	6	119	well & working
45	yes	no	M	46	sq.	no	no	8	118	well & working
54	yes	yes	M	51	sq.	no	no	2 yrs +	113	well & working
64	yes	yes	M	52	adeno-carcin.	no	no	52	89	well & working

TABLE 23. - Individuals surviving on 30-9-57, out of 123 cases of bronchial carcinoma diagnosed during 1955.

Table 23 shows that six of the 13 operated cases are alive with an average survival period of 116 weeks. Five of these are very well and working. Their average age is 52 years compared with 54 years for all operated, and 61 for all male cases. The histology of the 6 operated survivors was squamous 4, adenocarcinomas 2, and 5 had been free from involvement of the mediastinal glands at operation.

The 110 non-operated cases occurring during 1955 were all dead by mid 1957 with the exception of three. Two of these survivors by that time were very ill, and the third, a coin shadow case who refused investigation was very gradually deteriorating. Some further particulars of these three cases are given in Table 23.

There were by mid 1957 7 operated non-survivors; two undifferentiated, four squamous and one adeno-carcinoma.

Two did not appear to have any malignant mediastinal glands at operation. One of these two, a squamous case, died 13 weeks post-operatively with a complicated broncho-pleural fistula. The other had histologically a very undifferentiated malignant lesion. After a spell back at work he developed secondaries in the liver and spine and died 87 weeks post-operatively.

The other five cases had involvement of the mediastinal glands at operation and died with disseminated lesions 15, 32, 34, 38 and 84 weeks after the operation.

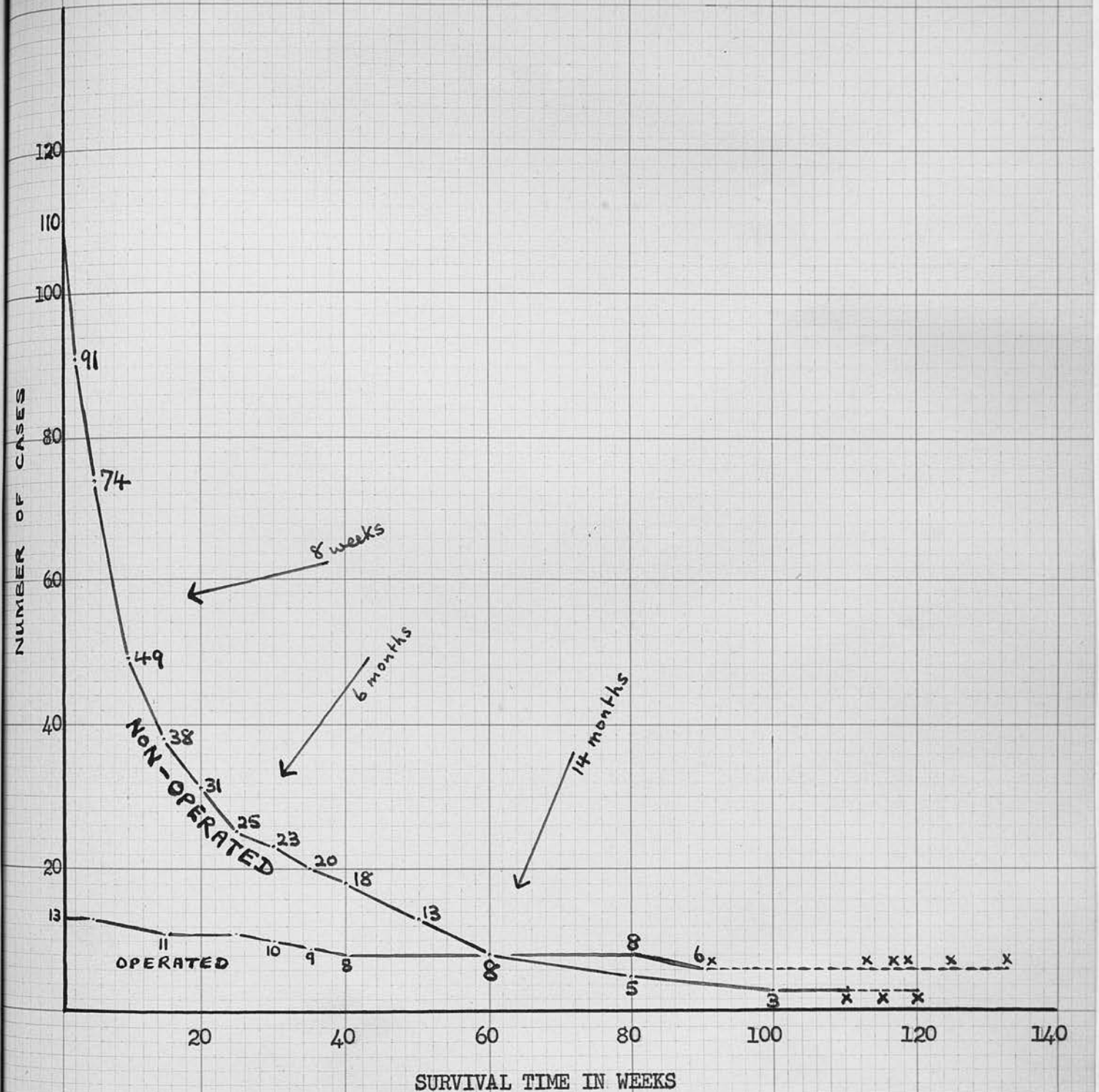
A fourteenth case of squamous histology, had too widespread lesions at thoracotomy to permit of resection. He died 28 weeks later, and is included in the non-operated group.

Table 24 shows the actual surivial time, in weeks from diagnosis, for both operated and non-operated non-survivors. It also gives the survival time up to mid 1957 for the non-operated and operated survivors.

The survival time of the operated and non-operated groups is further compared in Fig. 10.

SURVIVAL TIME	NON-OPERATED		OPERATED	
	DIED	SURVIVORS	DIED	SURVIVORS
1 - 2 weeks	19	91		13
3 - 5	17	74		13
6 - 10	25	49		13
11 - 15	11	38	2	11
16 - 20	7	31		11
21 - 25	6	25	1	11
26 - 30	2	23	1	10
31 - 35	3	20	1	9
36 - 40	2	18	1	8
41 - 50	5	13		8
51 - 60	5	8		8
61 - 80	3	5		8
81 - 100	2	3	2	6
101 - 120				
121 - 140				
TOTAL	107	3	7	6

TABLE 24. - Survival time, in weeks from diagnosis, for 110 non-operated and 13 operated cases.



x Correct survival point for each individual operated survivor
x Correct survival point, non-operated survivors

FIG. 10. – Survival time, in weeks from diagnosis, for 13 operated and 110 non-operated cases of bronchial carcinoma.

Fig. 10 shows that half of the non-operated cases were dead in eight weeks from diagnosis, and three quarters of them in six months.

After about a year or fourteen months the non-operated survivors fell below the operated survivors, although the non-operated cases numbered eight times more than the operated cases to start with. In less than two years the operated group was reduced to half its original number.

Roughly speaking the 123 total cases give a 7.5% two year survival rate, of which the operated cases make up 5% and are mainly well and working. The non-operated survivors who make up the other 2.5% are ill and deteriorating but not as rapidly as might be expected.

There are few published results relating to the average survival rate of un-operated series. My average for 110 non-operated male and female cases is 16.7 weeks, with three survivors after at least 21 months.

The survival period for the 7 operated non-survivors was 43 weeks.

These figures are shown in Table 25 together with the number of survivors and the survival period of the deceased members of various other groupings of the cases.

	GROUP	No. of Cases			% of group alive	Average survival of deceased cases, wks. from diagnosis.
		In Group	Alive after at least 21 mos.	Dead		
	All cases	123	9	114	7.3	18.4
	All male cases	102	8	94	7.8	18.7
	All female cases	21	1	20	4.8	16.7
1.	Male op. adeno-ca. without med. gl.	2	2	0	100.0	-
2.	" " sq. " " "	4	3	1 (1)	75.0	14 (1)
3.	Total male op. without med. gl.	7	5	2	71.0	50
4.	Male all operated	12	6	6	50.0	44
5.	All operated	13	6	7	46.0	43
6.	All cases c no evidence of met. (3)	20	7	13	35.0	54
7.	All operated c secs. in med. gls.	6	1	5	17.0	40
8.	All non-op. deep X-Ray cases	7	1	6	14.0	37
9.	All cases age 46 - 60	56	8	48	14.0	22
10.	All cases c history over 2 yrs.	31	3	28	10.0	22
11.	All male cases	102	8	94	7.8	18.7
12.	ALL CASES	123	9	114	7.3	18.4
13.	All cases c effusion on diag. (4)	19	1	18	5.3	12
14.	Female non-operated	20	1	19	5.0	15.6
15.	All female cases	21	1	20	4.8	16.7
16.	All non-operated	110	3	107	2.7	16.7
17.	All c metastases on diagn. (3)	88	2	86	2.3	12
18.	Male non-operated	90	2	88	2.2	17
19.	All over 60 years	62	1	61	1.6	14
20.	Male op. undiff. without med. gls.	1	0	1	0	87
21.	Male non-op. adeno-carcin.	2	0	2	0	49
22.	Female op.	1 (2)	0	1	0	38
23.	Male non-op. squamous	18	0	18	0	26
24.	All under 46 years	5	0	5	0	20
25.	Male non-op. undiff.	9	0	9	0	10
26.	Diagnostic necropsies (5)	10	0	10	0	3

(1) Post-operative death. (2) Only 1 female op. case.
(3) Table 18. (4) Ch. 11. (5) Ch. 7.

TABLE 25. - Survivors and survival periods (in weeks from diagnosis) for various groups of cases of bronchial carcinoma.

The number of cases in some of the groups in Table 25 is of course, too small to allow conclusions to be drawn. For instance there was only one female operated case, an adenocarcinoma, and she was unfortunately found to be very advanced at operation. Again one of the four male squamous cases without mediastinal involvement died post-operatively from a broncho-pleural fistula : otherwise his prognosis was expected to be good.

Table 25 however, may be interesting as a general picture. Generally speaking all the operated groups including those with nodal involvement (except the undifferentiated group), and all cases free from metastases on diagnosis, and even the age group 46-60 taken as a whole did better than the average.

On the other hand, undifferentiated cases, whether operated on or not ; cases with metastases on first diagnosis, cases with an effusion, female cases generally whether operated on or not, and all cases in the age groups under 46 or over 60 seemed to do less well than the average.

As might be expected, acute hospital admissions requiring necropsies for diagnostic purposes give the shortest survival period. As previously stated in Chapter 7, I regret I cannot give the histology of these, perhaps they contain a high percentage of undifferentiated cases.

In women and the under 40 groups Bignall (1955), and Nicholson et al. (1957), found more undifferentiated cases. The latter found only 7% of their operated cases consisted of women. This compares with necropsy and death rate figures of 15% to 24%, (see Bignall (1955), and Table 33).

The general experience among thoracic surgeons with regard to female cases generally and the under 40 age group seems to be one of disappointment and reluctance to undertake operation even in the presence of good general condition, a # one-year survival period after operation being a common outcome, and this of course is no use to anyone.

The number of adeno-carcinomas in my series is too small to justify what appears on the surface to be good results. Again the survivors in this series have not been followed up long enough. Nicholson et al. (1957), agree with Holmes Sellars that for a feeling of security, when judging the effects of treatment, a period of three years must elapse.

As stated in Chapter 10, I would not be certain of the anatomical position of origin of the tumours in more than a few cases so I could not study the effect of this on prognosis.

From the literature it would appear that carcinomas are about equally divided between the two lungs and according to Nicholson et al. (1957), they occur in the upper and middle lobes about twice as frequently as in the lower lobes.

Bignall and Moon (1955), and Noël (1956), found that the upper lobe lesions carried, operatively, a slightly better prognosis than lower lobe tumours, especially left lower lobe tumours. These drain towards the abdomen as well as to the right para tracheal lymph glands, which are not accessible at operation. If spread has taken place from upper lobe tumours the recurrent laryngeal nerve may be affected or the supraclavicular glands palpable, and the case rejected for surgery.

Tumours sited peripherally in the lung may be picked up in a very early state by mass radiography, and these, in the form of coin shadows, then carry a good prognosis operatively.

Nevertheless peripheral lesions are more silent than central lesions situated near the root of the lung, and in the absence of an X-Ray, they may spread by lymphatics, veins ~~viens~~, and perivascular lymphatics both centrally and peripherally. Centrally placed lesions, on the other hand, are more likely in an early stage to give rise to symptoms due to pressure, bronchial blockage, or infection, which may call attention to the lesion.

It was previously considered that 80% of lesions or more were situated near the hilus but recently Walter and Pryce (1955), on the basis of 207 resected specimens have suggested that in 53% of these, admittedly selected cases, the site of origin was peripheral. They consider that the central type is favoured for resection and that the

figure for lung cancer as a whole would be higher than 53% peripheral, and that the frequency of the peripheral type is a major factor responsible for the low operability rate and poor prognosis.

The survival period in relation to the duration of symptoms before diagnosis has been discussed in Chapter 6 and Chapter 9.

Fig. 11 shows the duration of symptoms against survival time for both operated and non-operated cases. Minimum figures have been taken for the duration of symptoms.

The height of the blocks of cases above the line represents average periods of symptoms of 3, 7, 13, 25, 34, 45, 61, 104 and 221 weeks. Below the line the average survival period for these blocks is shown to be 4, 17, 18, 13, 15, 30, 8, 24 and 8 weeks. The operated cases are shown individually in green. It will be seen that the average survival period of the non-operated is fairly constant throughout whatever the duration of symptoms. Nor is there a cluster of operated cases among the cases with a short or moderately short period of symptoms, in the fact the two operated cases with the shortest history did badly. The ten cases with a history of only 3 weeks who survived only 4 weeks were mostly terminal neglected cases, that came to my knowledge after death when it was too late to obtain a complete history.

The 31 cases with a history of possibly over 2 years (Table 21, P. 107), are included in the blocks with minimum periods of symptoms; they are shown again in red. Their average survival period was only 22 weeks, but three of them are still alive.

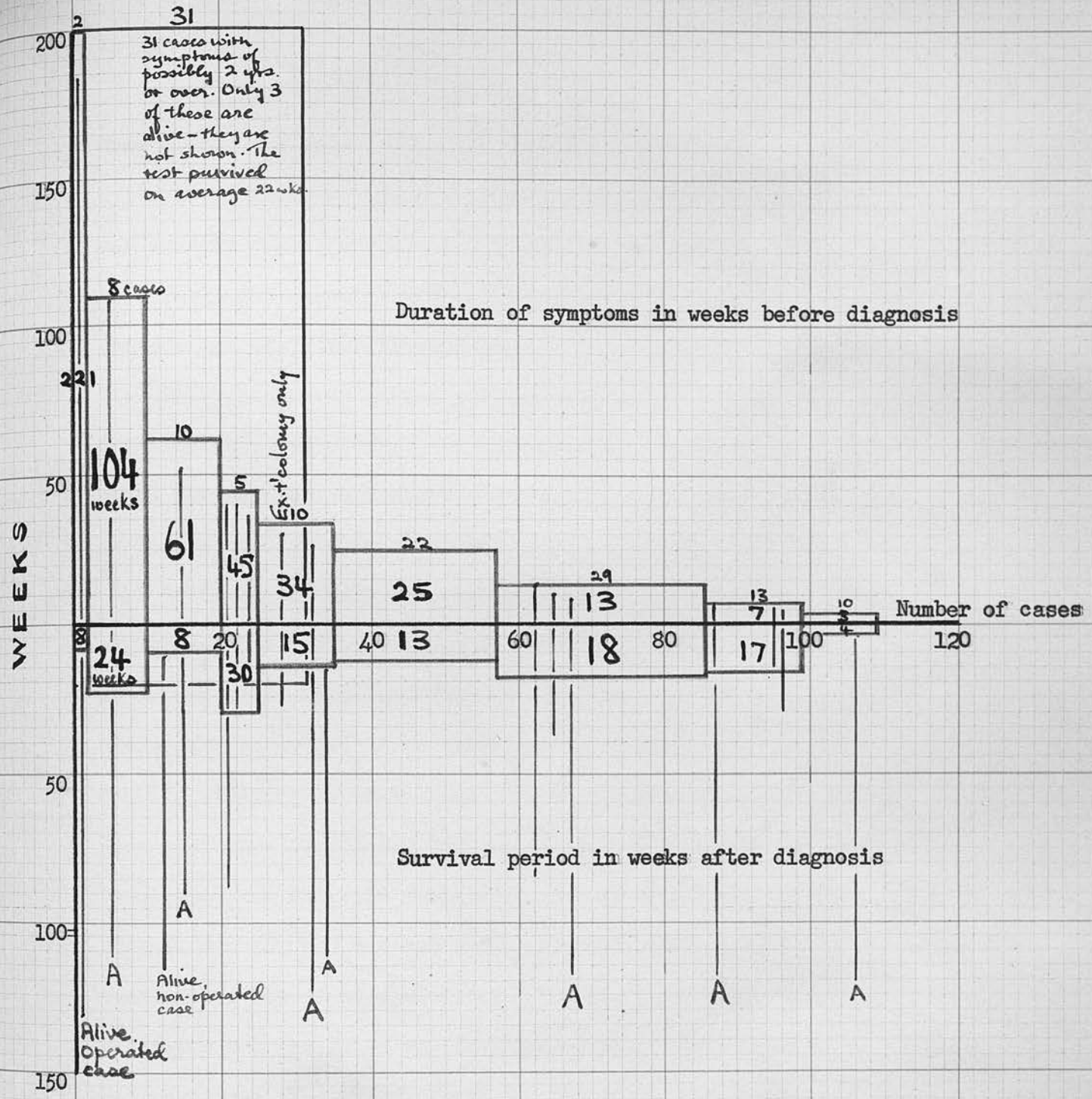


Fig. 11. – Diagram showing survival period according to duration of symptoms. The blocks above the line show groups of non-operated cases with about the same duration of symptoms, the survival period of each block being shown below the line. Their survivors are shown in red.
Operated cases are shown separately in green.
The duration of symptoms used has been the minimum definitely related to the carcinoma, but 31 cases with symptoms of possibly over two years are shown separately.

Eight (7%) of the non-operated cases had been given deep X-Ray therapy. One of these is alive but ill. The other seven survived on an average 37 weeks from diagnosis but only 18 weeks from the completion of treatment.

The eight cases consisted of 5 males and 3 females, of average age 49 years for both sexes.

The reasons for giving radiotherapy were:- Chest infiltration, two cases; root glands, four cases; vena caval obstruction, one case; and inability to operate because of an aortic lesion in the eighth case.

In three of these cases the histology was vague but suggested an undifferentiated lesion likely to be sensitive. In one case the histology was unknown, one case was an adeno-carcinoma, and three cases were squamous.

In addition to these eight cases, three cases were given post-operative deep X-Ray therapy as part of a random sample trial with the Christie Hospital. Two of these were males aged 51 and 52, who did not appear to have any involved mediastinal glands at operation. One was a squamous ~~called~~ -celled carcinoma and the other an adeno-carcinoma. Both are well and working. The third operative case given deep X-Ray therapy was a female aged 56, with an adenocarcinomatous growth involving glands and infiltrating mediastinal structures. She died 28 weeks from diagnosis.

Abbey Smith (1954) described several untreated cases surviving up to three years and we have had one or two surviving four years in a state of increasing invalidism.

Almost all of the satisfactory long surviving patients however have been operated cases, and operative survival rates were discussed in Chapter 6.

Most clinics now have cases surviving 5 years, 7 years, and even 10 years. Holmes Sellors in 1954 recorded one case surviving 15 years. Brewer (1956), referring to Graham and Slingers original case stated "Since the first patient to undergo pneumonectomy, performed in 1933, is still alive and apparently cured, we know that as long as cancer is confined to the lung, cure is possible by pneumonectomy."

CHAPTER 13

DEATH CERTIFICATION

At the end of Chapter 4, a possible diagnostic error of ± 10% or more, was postulated with regard to the 123 cases of bronchial carcinoma in this series. This error is of course passed on to the death certificate.

Among the recommendations of the symposium on Cancer of the Lung held at Louvain under the auspices of the C.I.O.M.S., in 1953, (Clemmesen 1954a), the most stressed was the need for accutate criteria on which to base the diagnosis. They divided the validity of diagnosis into three classes:-

CLASS I :- Positive result of histological examination of primary tumour of the lung,

or positive result of histological examination of secondary tumour, and evidence of primary tumour of the lung by radiological examination, bronchoscopy or thoracotomy,

or positive result of cytological examination and evidence of primary tumour of the lung by radiological examination, bronchoscopy or thoracotomy,

or autopsy.

CLASS 2 :- Positive result of cytological examination only,

or positive result of radiological examination only,

or positive result of bronchoscopical examination only,

or positive evidence at thoracotomy without biopsy.

CLASS 3 :- Evidence based on case history and physical examination; death certificate as only evidence.

According to this classification my series of 123 cases would be comprised as follows:-

	Male	Female	Total
CLASS 1	53	7	60
CLASS 2	43	13	56
CLASS 3	6	1	7
TOTAL	102	21	123

When trying to fit my cases into this classification, two difficulties seemed to occur:-

1. Cytological examination of pleural fluid, and to a lesser extent of sputum, plus radiological examination does not constitute certain class 1 evidence, and should, in my opinion, be put in Class 2.

2. Radiological examination alone, as in class 2, is very subjective in its interpretation and should, in my opnion, be placed in an intermediate class between classes 2 and 3. If the C.I.O.M.S. classification were adopted generally, perhaps in association with compulsory

notification (see Chapter 15, P. 196), then the very existance of an X-Ray would be considered as a support of the diagnosis.

The new classes would then be :-

CLASS 1. As before minus "cytology plus radiography."

CLASS 2. As before plus "cytology plus radiography," and minus "radiography alone."

CLASS 3. Radiography, history and clinical examination.

CLASS 4. As original class 3.

For research purposes class 4 would have to be disregarded where possible. In fact I DO NOT CONSIDER THAT CANCER OF THE LUNG SHOULD EVER BE DIAGNOSED ON THE GROUNDS OF HISTORY AND CLINICAL FINDINGS ALONE.

A certain amount of research could be satisfactorily carried out by using cases falling into classes 1 and 2 only, e.g. treatment follow-up, pre-diagnostic of history, and the study of certain etiological factors.

Other studies such as general epidemiology, would by definition have to use classes 3 and 4 as well.

If notification were made compulsory the numbers in these groups might perhaps be reduced. At the same time the true histological pattern of the disease might gradually become more apparent.

It is doubtful, however, whether compulsory notification would lead to cases being diagnosed earlier. (See Chapter 15, P.196).

The extent to which death certification agrees with reality has been studied by McKenzie (1956). He dispatched 770 inquiries to General Practitioners and received 654 replies, of which only 3% showed the cases to have been quite unconfirmed. 56% of the cases were considered to have been confirmed by a technique that permitted of the minimum of error.

One wonders, of course, whether a bias has been introduced here. Perhaps the 116 non-replies were due to reluctance to disclose lack of information.

On my series, only 40% of the cases were confirmed histologically (see Chapter 8), and only 54% histopathologically.

Although conditions now exist whereby the disease might be overdiagnosed or used as a spot diagnosis, Fullerton (1956), on the basis of necropsy studies, believes that the disease was under-diagnosed in the past and is still being underdiagnosed, (see Chapter 7, P. 77).

This view is also held by Steiner (Clemmeson 1954b), Pascua (1956b), Kotin (1956), and Rigdon and Kirchoff (1952).

As stated in Chapter 7, only 37% of my cases died in hospital.

CHAPTER 14

FACTORS OF POSSIBLE CAUSAL SIGNIFICANCE

It was originally intended to examine in detail factors of possible causal significance, but in many cases the patient either died before I could interview him or was too ill to give accurate details. Even simple facts such as smoking habits in young adult life, previous employment and places of residence and previous chest illnesses were difficult to establish. Relatives made unreliable witnesses.

The numbers being small I have decided simply to state the findings with a minimum of comment.

The factors dealt with will be:- age, sex, smoking, previous chest illnesses, place of living, occupation, apparent endocrine type, and social class.

1. AGE

The average age of the total cases was 61 years. Of the 102 male cases 61 years, and of the 21 female cases 63 years. The average age of lung cancer cases does not appear to have changed in England and Wales during the last 35 years.* The incidence in all age groups has increased and there is a continuing increase in ageing cohorts.

The actual age sex distribution of the 123 cases is shown in Table 26.

* Doll (1953 b), states that the maximum mortality in 1931-47 was a decade earlier than in 1953.

AGE	NO. OF CASES		
	MALE	FEMALE	TOTAL
1 - 35	0	0	0
36 - 40	2	0	2
41 - 45	3	0	3
46 - 50	8	4	12
51 - 55	16	0	16
56 - 60	27	2	29
61 - 65	18	8	26
66 - 70	11	1	12
71 - 75	10	3	13
76 - 80	5	3	8
81 - 85	2	0	2
TOTAL	102	21	123

TABLE 26. - Carcinoma cases by age and sex.

Table 26 shows that the main age group is 50 to 70. There were only 5 cases in the age group 45 and under. There were however 23 cases aged over 70.

Table 4 shows that for both males and females the cases verified histo-pathologically are on the average 10 years younger than the cases that are not, even although the former group contains a number of older cases verified at necropsy. This suggests that the older group is too ill on diagnosis for investigation.

The fact that the average age of onset in females is no less than in males does not support the view that the disease in females is connected with menopausal endocrine changes.

In England and Wales during 1954 2% of the deaths from lung cancer occurred in 308 persons under 40 years of age. The sex ratio, M:F of these cases was 3:1 which is considerably less than the ratio for older people. It is believed (Lancet Edit. 19-5-56) that in these cases there is an excess of adenocarcinomas and undifferentiated cases and a reduction in the proportion of the squamous type.

Unlike most other forms of cancer, the rates decline after a certain age, yet in men born in the same decade the death rate continues to rise with advancing age and men born in each successive decade have higher lung cancer death rates than their predecessors when they reached the same age.

2. SEX

The male/female ratio in this series is 102 to 21 or 5 to 1.

Among the women the diagnosis was rather more difficult to establish, a doubt existing in 35% of the female cases compared with 27% of the male.

For the histo-pathologically confirmed group the ratio was 57 to 9 or 6 to 1. For the 13 operated cases the ratio was 12 to 1 and for the one year survivors it was 6 to 1.

Among the 29 proved squamous cases the ratio was 6 to 1, among the 5 adenocarcinomas 4 to 1, and among the 14 undifferentiated cases also 4 to 1.

Among my 131 non-carcinoma cases a quite similar sex ratio was observed of male to female 5 to 1. I believe that although the death rate from respiratory disease is of the ratio, male to female, of 3 to 1 (Martin 1957), the morbidity ratio is much higher.

3. SMOKING

The smoking habits of the 123 cases, as far as could be determined, are shown in Table 27.

Table 27 shows that among the 102 male cases there were no non-smokers, and indeed no cases smoking less than 10 cigarettes a day. There were only 20 male cases smoking less than 20

GROUP	No. of Cases	SMOKING HABITS									
		CIGARETTES								Pipe only	Cigars
		30+	25+	20-24	15-19	10-14	5-9	1-5	0		
Total Cases	123	35	12	35	7	18	3	4	7	2	
male	102	35	11	34	5	15				2	
female	21		1	1	2	3	3	4	7		
Verified histologically											
male	41	14	5	13	3	5				1	
female	8			1	1	2	1	1	2		
squamous											
male	26	8	2	9	2	4				1	
female	4				1	1	1		1		
adenocarcinomas											
male	4	2		2							
female	1			1							
undifferentiated											
male	11	4	3	2	1	1					
female	3					1		1	1		
Males under 56	28	8	6	7	3	4					
over 65	27	8	3	11	3	2					

TABLE 27. - Smoking habits of 123 carcinoma cases by various groups.

cigarettes a day. Only two of the male cases smoked a pipe only.

Among the total 21 female cases there were 7 non-smokers but only 2 among the female histologically confirmed cases. One of these was a squamous type of growth, the other anaplastic.

There was no difference in the amount smoked between 28 male cases under 56 years, and 27 male cases over 65. This suggests that age of onset is not directly proportional to the amount smoked.

Lutwyche found 2 non-smokers among 116 cases at the Willesden Chest Clinic (22 of his cases however had no record of smoking habits).

I have no figures relating to the smoking habits of my controls.

Figures however are available, (James 1957), regarding the smoking habits of the population of this country by age and sex, as compiled by the Tobacco Manufacturers Standing Committee, (James 1957). These figures indicate that 78 to 79% of males aged 45 to 74 are cigarette smokers, the percentages being less for the younger age groups. The average consumption per smoker is from 12 to 17 cigarettes a day. According to the Hulton Readership Survey, (Hansard 1957), 66% of males over 16 years smoke an average of 15 cigarettes a day, which is a similar finding and much less than the percentage of persons smoking

and the amount smoked by the patients in the present series.

According to Haenszel and Shimkin, (1956), in the United States 30.9% of males aged 45 to 54, 41.1% of males aged 55 to 64, and 65.1% of males of 65 years and over have never smoked cigarettes regularly. This indicates considerably less smoking than in England and Wales and shows a great difference from the habits of the cases in this series.

According to James (1957) from 24% to 37% of women aged 45 to 74 in England and Wales are cigarette smokers, the amount smoked varying from 4 to 9 cigarettes a day. This again is considerably less than in my series.

4. PREVIOUS CHEST ILLNESSES

As shown in Table 21, Chapter 9, 31 of the 123 carcinoma cases gave a more or less continuous history of chest illness for two years or more prior to the diagnosis of the carcinoma. In fact the average duration of their symptoms was 14 years. Some went back as far as 30 years, and some of these had had other chest illnesses before that.

Two cases have been described in detail (Fig. 4 Chapter 3, and Fig. 9 Chapter 11) which show a gradual almost imperceptible transition over a number of years from chronic bronchitis into carcinoma.

In addition to these 31 cases there were another 16 cases with a history of chronic chest symptoms (perhaps slight), for

many years, but not continuous with, or quite the same, as those relating to the carcinoma.

There were yet another 23 cases with a definite history, years before, of short period acute chest illness or intercurrent chest infection.

This makes a total of 70 cases with a history of previous chest illness, which is 57% of all the carcinomas.

Case and Lea (1955), believe that lung cancer and bronchitis occur together more often than would be expected by chance. They found twice as many deaths from lung cancer among men pensioned from the Army with bronchitis, than among a similar general population group.

Similarly Raeburn and Spencer (1957), believe that reparative hyperplasia of small bronchioles, in response to chronic inflammation, may progress to malignant change.

Auerbach (1957), describes an excess of changes such as basal cell metaplasia, squamous metaplasia, and carcinoma in situ among heavy smokers and lung cancer patients.*

5. PLACE OF LIVING

A note was made of the place of residence of each case but the number of country dwellers was very small. It was not possible in respect of the others to obtain details of their exposure to smoke and road fumes over the years.

Enquiries regarding place of residence as well as enquiries related to smoking habits, would be more easily carried out among patients attending surgical clinics, where they would all be available for repeated interviewing.

* Auerbach, O. (1957). Tuberc. & Dis. Chest, 4, 290.

6. OCCUPATION

Occupational details of all abnormal cases found by mass radiography have been rendered to the Ministry of Health since 1942. Analysis of the occupations of the bronchial carcinoma cases has not revealed any set pattern of general etiology. Isolated instances in factories dealing with copper sulphate, nickel, arsenic, chromate, and asbestos have been described as well as among gas works stokers and coke oven chargers (Clemmeson 1956c).

There is, however, a striking difference in the occupational exposure to smoke between the two sexes. Thus of the 102 men, 60 were exposed to considerable smoke at work as is shown in Table 28.

There was one electroplater in this series and from the same small works one other case occurred a few years ago.

The industrial process consists of cleaning sheet metal in tanks containing 880 gallons of HCl. It is then heated and dried and dipped in pure zinc at 450°C. It is then sprinkled with ammonium chloride. All three processes give rise to heavy fumes to which the workers are exposed. As far as I know however this process does not involve nickel, chromates, arsenic or copper.

OCCUPATION	NO. OF CASES
Garage workers or aero engineers	7
Painters	5
Railway workers	5
Motor or lorry drivers	4
Gas workers	4
Quarrymen	4
Boilermen	4
Miners	3
Wood varnishers or French polishers	2
One each: blacksmith, iron turner, steam roller driver, iron molder, plumber, battery filler, power station worker, fireman, electroplater.	9
Various other labourers in smoke	13
TOTAL	60

TABLE 28. - Occupations involving smoke among 123 cases of carcinoma.

7. ENDOCRINE BALANCE

At the outset of this survey it was proposed to record any endocrine peculiarities met with, and also, if possible, to assess the sex activity of the patient.

From previous experience it seemed that these patients were a little lethargic, slow, unanxious, unambitious and over-weight and one wondered whether they might be of the hypothyroid type. This possibility has been mentioned by Handley (1955), Spencer (1954), and Loeser (1954).

A complicated list of allegedly hypothyroid signs and symptoms was made out and about 20 estimations of fasting serum cholesterol were done. However no definite pattern emerged nor any obvious deviation from the wide limits of normal.

Similarly among the females it was at first thought that they showed a personality change towards the male type, being of the hirsute, organising, businesslike, masculine, smoking type - but this again could not be considered general.

As shown in Table 26, P. 149, only 4 of the 21 female cases occurred in the under 56 age group, in which menopausal changes might be expected.

With regard to marital state no definite pattern emerged.

Of the 57 cases confirmed histo-pathologically 48 were married and all these except 7 had children. Seven were widowers and two were single. The other cases were similar;

there was no sign of sub-fertility during their early and middle life.

8. SOCIAL CLASS

It is difficult to assess the proportion of patients in the different social classes when dealing with small numbers in an industrial area.

I agree with Brett et al.(1956), who found a statistically significant higher rate in Social Class $\overline{V}$ among 62 cases diagnosed at the Islington Mass Radiography Unit.

Clemmesen (1954d), in Copenhagen also found a slight excess of bronchial carcinomas among the lower social classes.

CHAPTER 15

DISCUSSION

In this chapter I would like to discuss six main problems as follows:-

1. Is the increase of the disease real?
2. The different incidence in the two sexes.
3. Possible carcinogens, especially smoking and atmospheric pollution.
4. Hormone dependency.
5. Early diagnosis and the possible existence of an antecedent silent period.
6. Compulsory notification and cancer registration.

1. IS THE INCREASE OF THE DISEASE REAL?

The main assessment of the incidence of the disease is made from death certificates, but over the last 60 years the classification used has frequently been changed.

In the Registrar General's Annual Reports and Statistical Reviews for England and Wales, deaths from cancer of the lungs, bronchus and pleura have been distinguished since 1897, the form of presentation of cancer deaths by site being re-arranged in 1901 after consultation with the Cancer Investigation Fund, (about the same time as the Imperial Cancer Research Fund came into being).

Cancer of the respiratory system was not distinguished in the International Classification of Causes of Death until the 4th Revision in 1929, and cancer of the lungs and pleura was not distinguished in the International Classification until the 5th Revision in 1938, when the group included the mediastinum.

The present International Classification categories date from the 6th Revision in 1948 when categories 162 and 163 were introduced dividing neoplasms of lung, bronchus and pleura into primary and secondary, the groups being now as follows:-

No 160. Malignant neoplasms of nose, nasal cavities, middle ear, and accessory sinuses (tumours of the skin of these organs excluded).

No 161. Malignant neoplasms of larynx.

No 162. Malignant neoplasms of bronchus, lung, or pleura, specified as primary, and of trachea.

No 163. Malignant neoplasms of lung and bronchus and pleura, unspecified as to whether primary or secondary.

No 164. Malignant neoplasms of mediastinum.

No 165. Malignant neoplasms of thoracic organs (secondary).

In spite of the periodic narrowing of the definition of cancer of the respiratory system there has been an absolute increase in the mortality from primary lung cancer from 2293 deaths in 1925 to 18185 deaths in 1956 in England and Wales, an increase of 800%.

The figures for the intervening years taken from the Registrar General's Statistical Reviews are given in Table 29, together with the annual deaths from some other causes that have greatly changed during these years.

YEAR	ENGLAND AND WALES		
	Total Population	No. of Deaths from	
		Lung CANCER	Respiratory TUBERCULOSIS
1925	38,890,000	2293	32382
26	39,067,000	2394	30108
27	39,290,000	2450	31055
28	39,482,000	2692	29799
29	39,607,000	2751	31425
1930	39,947,931	3122	29414
31	39,952,377	3440	29658
32	40,201,000	3608	27627
33	40,350,000	3852	27854
34	40,467,000	4229	25682
35	40,645,000	4513	24603
36	40,839,000	4871	23015
37	41,037,000	5251	23215
38	41,215,000	5805	21282
39	41,399,000	6124	21523
1940	41,862,000	4815[1]	23470
41	41,748,000	4990	23339
42	41,897,000	5596	20730
43	42,259,000	6109	20924
44	42,449,000	6568	19815
45	42,636,000	7161	19668
46	42,737,000	8044	19008
47	43,050,000	9204	19573
48	43,502,000	10162	18798
49	43,785,000	10975	17471
1950	43,830,000	12241	14079
51	44,008,000	13247	12026
52	44,166,000	14218	9335
53	44,301,000	15128	7913
54	44,480,000	16331	7069
55	44,623,000	17271	5837
56[2]	44,667,000	18185	4849
57			
58			
59			

1. Excluding larynx and mediastinum.

2. Provisional, from Registrar General's Quarterly Return, 1st. Qtr. 1957.

YEAR	ENGLAND AND WALES			
	Number of deaths from			
	PNEUMONIA	BRONCHITIS	INFLUENZA	Senility and Ill-defined diseases.
1925	36990	35252	12721	25314
26	32339	30187	8936	24564
27	37242	33021	22263	22753
28	31014	23431	7754	19750
29	43846	33378	29084	21180
1930	27724	19523	5019	18117
31	33573	25160	14409	17987
32	29558	20334	13156	18266
33	30095	21075	22890	17138
34	28623	18948	5619	16066
35	26786	15762	7382	16993
36	28890	34216	5778	17286
37	30331	35411	17132	17168
38	27467	25954	4446	15399
39	23370	31423	8019	17267
1940	29007	46225	11420	18232
41	26286	34020	6866	17782
42	20683	26827	3382	15852
43	24638	31386	12576	16673
44	19930	27156	3876	16325
45	19052	28470	2669	16423
46	19132	27049	5272	15532
47	21533	30199	3303	14990
48	16883	23888	1238	11907
49	20132	28981	5592	12402
1950	17573	28257	3902	9716
51	22496	36985	15809	9480
52	18608	27268	1750	7574
53	20759	30392	6465	7477
54	18079	25543	1811	8185
55	20994	28793	2983	8981
56	22369	29663	2625	8333
57				
58				
59				

TABLE 29. - Population, 1925 to 1956, of England and Wales, and annual deaths from lung cancer, respiratory tuberculosis, pneumonia, bronchitis, influenza, and "senility and ill-defined diseases".

Absolute figures of deaths recorded are used because they are readily available, but they should be related by age and sex to the total population which increased from 38,890,000 to 44,667,000 from 1925 to 1956.

During this period also general mortality from all causes materially diminished, so the proportional representation of cancer in all the mortality would have increased somewhat, even if the absolute figures of mortality from cancer had remained stationary throughout the years considered.

Again the population is ageing with consequent swelling of the 40-80 age group, which is the lung cancer age group in all countries.

Pascua (1952) gives two tables which suggest some correlation between an ageing population and high percentage of deaths from all types of cancer, for 15 European and 8 extra European countries. In Table 30 it will be seen that Spain, Portugal, Chile and Japan in 1947 gave the lowest death rates from cancer, and they also gave very low figures for the proportion of persons over 60 years of age in 1949 as compared with 1900, but the question of the completeness of the death notifications in these countries must be considered.

In most countries with reliable statistics, cancer, which caused about 5% of all deaths around 1900, caused 10% to 16% of all deaths by 1947.

In Table 30 it will be seen that the Netherlands and Denmark in 1947 gave 16% of all deaths as due to cancer, these being the highest figures for the 23 countries mentioned, yet

in 1949 their increase of persons over the age of 60 for the preceding 50 years was surpassed by more than half these countries.

	% of all deaths due to cancer 1947	Increase per 1000 pop. of persons aged 60 yrs. or over 1900 - 1949
Netherlands	16.41	22
Denmark	16.19	32
Switzerland	15.74	45
Norway	15.32	26
E & W.	15.06	84
Germany	14.95	51
Uruguay	14.79	not known
New Zealand	14.56	69
Scotland	13.70	68
Canada	13.27	34
U.S.A.	13.13	52
Sweden	12.99	30
Australia	12.88	63
Union of S.A.	12.49	60
France	11.90	39
Belgium	10.12	64
Finland	10.09	26
Eire	8.99	39
Italy	8.50	22
Spain	5.91	19
Chile	4.82	-5
Japan	4.66	-6
Portugal	3.59	3

TABLE 30. - Deaths from all types of cancer in 1947, related to ageing of population 1900 - 1949 in 23 countries (Pascua 1952).

With regard to the possibility of the disease being underdiagnosed in the past, the evidence is largely indirect.

As stated in Chapter 7, some pathologists believe that the disease was, and still is, underdiagnosed. They point to the quite substantial incidence found by individual pathologists even in the 1880's (see Table 13).

Careful study in places where the disease has not been recorded, as greatly increasing, as in East Pakistan by IBRAHIM (1954), has revealed an unsuspected prevalence of the disease.

Steiner of Chicago has studied the etiological implications of the geographical distribution and this is summarised in his most interesting contribution to the C.I.O.M.S. Symposium (Clemmesen 1954e). He believes that "an increase in lung cancer disproportionate to that for all or selected types of cancer has not been demonstrated in most geographical regions, and perhaps even in none".

Doll (1953b) takes the opposite view and in that year enumerated his now famous "seven reasons" for believing that the observed increase in the disease is real.

The technical aids to the diagnosis of bronchial carcinoma have made great strides during the last sixty years. As far back as 1893 King and Newsholme pointed out that when a cancer site becomes accessible clinically during life an increase in the number of diagnosed cases is to be expected.

A comparison of the figures for the major causes of death in 1925 and 1955, as set out in Table 31 and Fig. 12 leaves little doubt that a transfer of cases to the lung cancer heading from the tuberculosis, bronchitis, pneumonia, influenza, and senility headings could have taken place unnoticed.

DEATHS 1925

England & Wales : Pop. 38,890,000

Registrar General : Statistical Review 1925, Table 4. Page 7
and Table XXXVII Page 38.

Total Deaths :- ~~472,841.~~ 474,350

1. Heart & C.V.S. (incl. cer. vas. accident & rheu. fever)	112,906	(98,699 in 1915)
2. Respiratory Diseases. (incl. influenza).	90,550	(118,404 in 1915) Pneu. 36990 Bron. 35,252 Influ. 12721
3. Cancer (~~incl~~ excl. br. car.).	51,155	Alim. 30653 Breast & Ut. 11116
4. T.B. (all forms).	40,387	
5. Alimentary Disease	27,511	Peptic ulcer 3452
6. Violence	18,314	
7. Endocrines, anaemias, ~~genall~~ genito-ur. excl (~~incl~~. prostate, cancer & rheu fever).	30,412	Diabetis 4357 Nephritis 12,615
8. Childbirth. New born.	22,731	
9. Fevers and Syphilis. (excl. T.B. and influenza).	20,794	
10. Hyperplasia of prostate	2,665	
11. Senility and all other causes incl. nervous diseases except c.v.a. (Senility and ill-defined diseases 25314).	54,632	
12. Cancer of "lung and pleura"	2,293	
	474,350 ~~472,841~~	

DEATHS 1955

England & Wales : Pop. 44,441,000

Registrar General : Quarterly Return, 1st. Qtr. 1956. No. 429
Table VI. P. 14. Total Deaths :- 518,865.

1.	Heart & C.U.S.	266,908	
2.	Cancer (excl. br. ca).	75,733	Alimentary 37,769 Breast & Ut. 12,436
3.	Respiratory Diseases	57,994	Pn. 20,994 Bronchitis 28,792 Influ.2,983
4.	Violence	21,468	
5.	Bronchial Carcinoma	17,271	
6.	Alimentary Diseases	16,193	Peptic Ulcer 5517
7.	T.B. (all forms).	6,492	
8.	Hyperplasia of prostate	4,090	
9.	Fevers and Syphilis (excl. T.B.)	3,187	
10.	Endocrines. Anaemias & Genital. (excl. prostate).	13,259	Diabetes 3284 Nephritis 4901
11.	Childbirth, new born.	14,193	
12.	Senility and all other causes. (Senility and ill-defined diseases 8981).	22,077	
		518,865	

TABLE 31. - Comparison of major causes of death, in England and Wales, in 1925 and 1955.

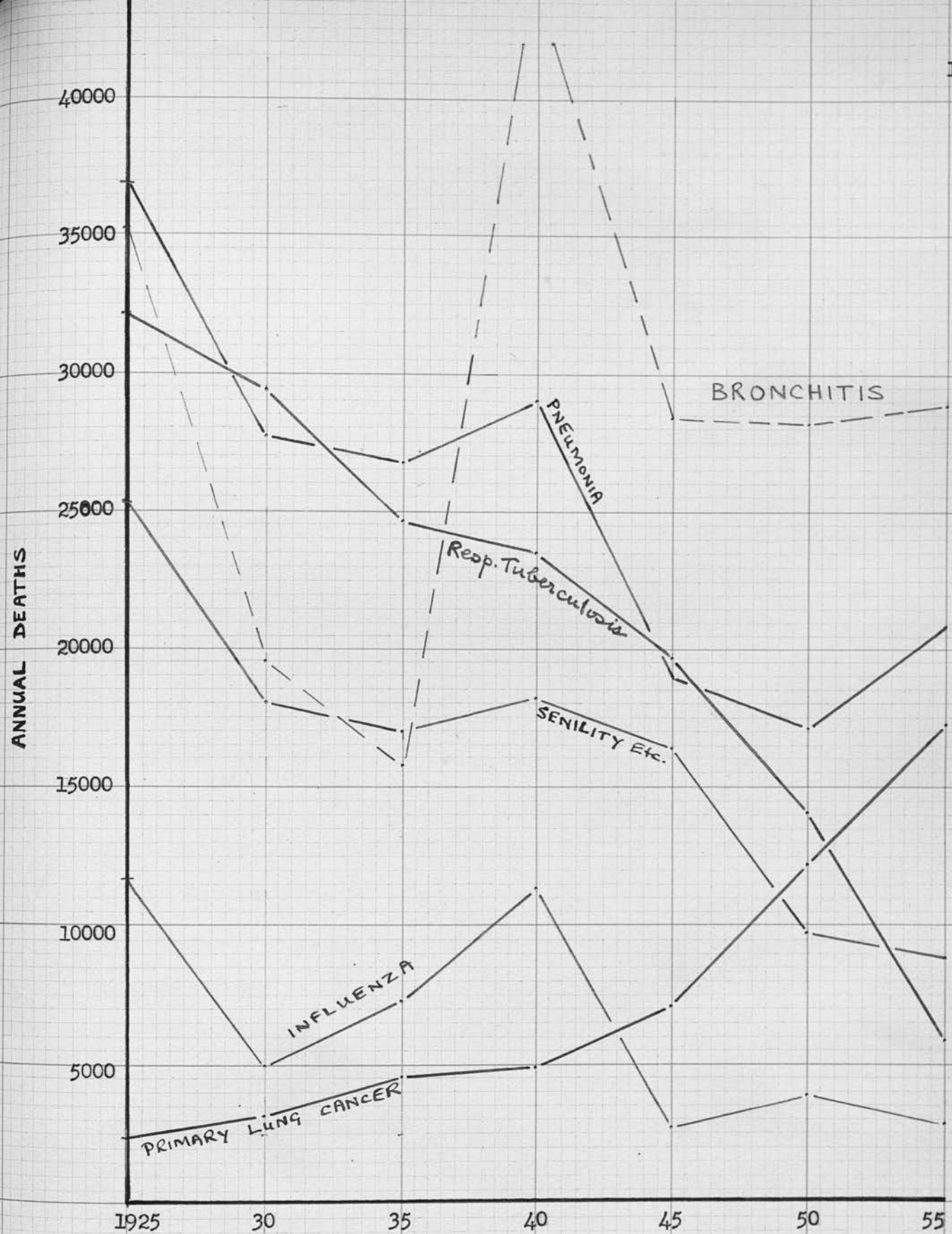


FIG. 12. – Annual deaths from lung cancer, respiratory tuberculosis, pneumonia, bronchitis, influenza, and "senility and ill-defined diseases", 1925 to 1955, at five yearly intervals.

Table 31 contrasts the main causes of death recorded in 1925 in England and Wales, with those recorded in 1955.

In 1925 lung cancer caused only 2293 deaths. By 1955 however it had become about the fifth single major cause of death, the figure having risen to 17,271. Thus it now accounted for over three times as many deaths as respiratory tuberculosis, nearly as many as pneumonia, and more than all the alimentary diseases combined (excluding neoplasms), but less than half of all alimentary neoplasms.

Between 1925 and 1955 tuberculosis (all forms) had fallen from the fourth major cause of death at 40,387 to a fairly low position namely 6492, comparable with such causes as peptic ulcer 5517, and non-malignant prostatic disease 4090.

The total number of deaths from respiratory disease, other than cancer and tuberculosis, fell from 90,550 in 1925 to 57,994 in 1955. Pneumonia caused 36990 deaths in 1925 and only 20,994 in 1955; the deaths from bronchitis fell from 35,252 to 28,792; and from influenza from 12,721 to 2983.

There are of course many causes other than more accurate diagnosis, for the fall in the number of deaths from respiratory disease, and this trend was under way during the period 1915 to 1925 before the deaths from bronchial carcinoma started rising materially. However, since 1925, in addition to the dramatic rise of 16,000 in the deaths recorded annually from bronchial carcinoma, there has been, as shown on Fig. 12, an equally dramatic, though more often forgotten, drop of over

75,000 in the deaths recorded annually from pneumonia, bronchitis, influenza, tuberculosis and the composite group, "senility and ill defined diseases".

Pascua (1952), states that during the last 30 years "there has been great reduction in deaths registered as due to "senility" and "unknown and ill-defined diseases". These "bag" rubrics comprised, in the past, many other miscellaneous pathological conditions which have also been affected by better diagnosis and better medical certification. The conviction is held by some competent analysts and research workers that this transfer has been one of the major factors contributing to the rise in recorded mortality from malignant neoplasms."

In contrast, Clemmesen (1954f), believes in a real increase in the disease whether due to recent customary, occupational, or hormonal causes. On the basis of cohort studies and ingenious international comparisons, and assuming that the cohort born in 1905 represents the final level of carcinogenic influence, he has made predictions regarding the future male mortality from cancer of the lung for Greater Copenhagen. He states that "by 1990, the number of deaths from cancer of the lung in the male population will amount to about 1000 against 168 in 1950, or 852 from all forms of cancer in men in 1950. It would seem not unreasonable to expect a similar development in the provincial towns and the rural areas, and among women."

2. SEX DIFFERENCES

In Chapter 14 the main sex differences observed in this series were discussed.

The increase in the recorded deaths from bronchial carcinoma seen in all countries for which statistics are available has been consistently more marked among males than among females as will be seen in Table 32, (after Pascua 1955a).

Although Table 32 shows a continued increase in mortality from bronchial carcinoma among females of quite a considerable extent in some countries, in those countries with stabilised statistics the increase is consistently less than for men.

This is brought out clearer in Table 33, which gives the ratio of male to female deaths for fourteen countries in the early 1930's and again in 1951 (Kotin 1956).

Dr. Pascua (1955b), states that levels of recorded mortality for either sex differ rather widely among the countries reviewed. He states that variations in medical facilities and practice may account for this, and that the proportion of the population living in urban and rural areas may also have a bearing of some consequence.

He is however impressed by the fact that in every country and in every year considered, the mortality is much greater in men than in women, sometimes five or six times as much. The rate of increase also being more marked for males. Dr. Pascua considers that these findings do not favour the hypothesis that the increase in mortality is merely due to improvements

COUNTRY	MALES	FEMALES
	% mortality increase 1949-1952	% mortality increase 1949-1952
Japan	68	83
Denmark	49	51
Eire	47	62
New Zealand	46	46
Italy	45	13
Germany	40	29
Scotland	36	nil
Norway	32	?
E & Wales	31	21
France	30	9
Finland	30	?
Switzerland	28	nil
Australia	25	?
Netherlands	24	nil
U.S.A.	21	10

TABLE 32. - Percentage increase in mortality from bronchial carcinoma 1949-1952 in males and females, for 15 countries. (After Pascua 1955a).

Ratio of Male to Female death rates with regard to cancer of the respiratory tract.

	Early 1930's	1951
Switzerland	6.0 : 1	6.1 : 1
Netherlands	3.3 : 1	5.8 : 1
Finland	5.9 : 1	5.8 : 1
E & Wales	3.0 : 1	5.4 : 1
U.S.A.	2.3 : 1	4.7 : 1
New Zealand	2.8 : 1	4.4 : 1
Scotland	1.9 : 1	4.3 : 1
Canada	2.1 : 1	4.2 : 1
Australia	2.7 : 1	4.1 : 1
Denmark	1.8 : 1	3.9 : 1
U. of S.A.	3.8 : 1	3.5 : 1
Italy	2.1 : 1	3.5 : 1
Eire	1.7 : 1	2.7 : 1
Norway	1.5 : 1	2.2 : 1

TABLE 33. - Ratio of male to female death rates from cancer of the respiratory tract in 14 countries, (Kotin 1956).

in diagnosis. He cannot understand why physicians should not diagnose malignant chest neoplasms in women as well as men. He conjectures that some real increase in broncho-pulmonary cancer has occured in men.

Mortality however from cancer of the so-called "accessible" sites such as nasal cavities, middle ear, simuses and larynx did not show any trend of increase during the four years 1949-52, in spite of the increase in smoking habits. In these diseases also the male to female ratio has remained constant.

The lower incidence of bronchial carcinoma among women has been interpreted in two different ways.

1. Some authorities consider that the possible causes of male lung cancer operate among females but to a lesser extent. For instance only half as many females smoke as males, and those who do, smoke only half or less as much, (James 1957). The ratio of the amount smoked is given as M to F, 5 to 1, which is similar to the observed sex incidence of the disease. Recently Wynder et al.* have reported an excess of smokers among women with bronchial carcinomas of the squamous and anaplastic types.

It is believed, as shown in Chapter 14, that women are protected to some extent from occupational smoke, and to a lesser extent from atmospheric pollution.

Women also are less subject to general respiratory disease, which may have a predisposing effect to cancer to some extent among males.

* Cited in Editorial (1957). Brit. Med. J., 2, 458.

2. Other authorities such as Nicholson et. al. (1957), go so far as to state that bronchial carcinoma in women might be regarded as almost a different disease.

The histology is different, there being generally a higher proportion of undifferentiated cases and probably adenocarcinomas. The number of squamous cases is less. More cases are seen among non-smokers. The course of the disease is generally less favourable than in males, and a much smaller proportion of cases are suitable for surgery. Nicholson et. al. (1957), found a M to F ratio of 13 to 1 among their operated cases.

Haenszel and Shimkin (1956), found that sex difference in the proportion of cigarette smokers narrowed in the younger cohorts. They found in the mortality from bronchial carcinoma a male excess that could not be accounted for by standardisation for smoking habits.

3. POSSIBLE CARCINOGENS; SMOKING AND ATMOSPHERIC POLLUTION.

As stated in Chapter 14 every one of my 102 males cases smoked, and only 20 of them smoked less than 20 cigarettes a day. Half of my male patients worked in unusually smoky jobs.

The study of carcinogens may be said to have started in 1775 when the English surgeon Percivall Pott ascribed

chimney-sweep's cancer to prolonged contact with soot.

A hundred years later skin cancer among the mule spinners of Lancashire and the shale-oil workers of Scotland was linked with oil. Further cancer hazards in industry due to dyes, radio-active ores and gases, radium, and chromates were later recognised, but it was not until 1915 that the first experimental production of malignant tumours, was announced by Yamagiwa and Ichikawa (Woglom 1926).

In 1922 Passey of Leeds showed that ethereal extracts of soot were carcinogenic, and the search for the specific chemicals was intensified, especially by Kennaway (1924) who was following up the work of Berthelot (1866), Schroeter (1920), and Bloch and Dreifuss (1921).

Several carcinogens were obtained by Kennaway and identified in conjunction with spectroscopic studies by Mayneord. By 1930 these workers had identified 3:4 benzpyrine in pitch, and it had also been synthesized in conjunction with Professor J. W. Cook. Hundreds of series of biological tests upon mice showed this to be the most powerful carcinogenic substance yet known (Kennaway 1955b).

A possible carcinogenic action by smoking or in tobacco was considered possible by Lombard and Doering (1928), and by McNally (1932). Among the first to describe a correlation between lung cancer and smoking was Muller (1939).

There were (and still are) very great difficulties in analysing tobacco smoke, but in 1951 Wedgwood and Cooper

announced a method of detection and determination of polycyclic hydrocarbons in micro-gram quantities by chromatography followed by absorption spectrometry.

Applying this method to the analysis of cigarette smoke, Cooper and Lindsey (1953), found anthracene and pyrene, and later Cooper et. al. revealed the presence of the carcinogen 3:4 benzpyrene previously mentioned, and known to occur in soot (Goulden and Tipler 1949), as well as other potential carcinogens, first in the smoke from cigarette paper (Cooper and Lindsey 1954), and later in cigarette smoke itself (Cooper, Lindsey, and Waller 1954, and Cooper and Lindsey 1955).

Cooper and Lindsey (1955), found that the smoke from 500 cigarettes gave 4 micro-grams of 3:4 benzpyrene. The figure from the laboratories of the Tobacco Manufacturers Standing Committee (1957), was almost the same, namely 3 to 5 ug per 500 cigarettes. A packed of 20 cigarettes would therefore contain .16 ug of 3:4 benzpyrine.

Cardon and Alvord of Rand Development, Atlanta (1956), gave 2.5 ug as the 3:4 benzpyrene content of the average cigarette packet - a much greater amount than that reported by Cooper et. al.

Cooper (personal communication), states that the hydrocarbons formed when a cigarette is smoked are highly unstable and at present we only know of two or three out of perhaps a possible 400. Filters are only about 10% effective and as the hydrocarbons are insoluble they cannot be removed

by bubbling through water, even though smoke particles are essentially droplets.

Cardon and Alvord (1956), believe that impregnation of cigarette papers and tobacco with ammonium salts may inhibit the formation of benzpyrene by as much as 60%.

Recently Wynder (1957) has suggested that the waxy coating of the tobacco leaf and stem is a major source of cancer-causing substances. This he believes may be able to be removed before manufacture.

Campbell and Cooper (1955), found 3:4 benzpyrene, in about the same concentration as in cigarette smoke condensate, in Zulu snuff which is associated with a high cancer incidence of the nasal sinuses.

Waller (1952), demonstrated the presence of 3:4 benzpyrene among the polycyclic hydrocarbons in the atmosphere of several British cities in concentrations up to 4.5 ug per 100 meters. The concentration was higher during the winter than in summer and four times higher in foggy weather than on clear days. Cooper (1954b), studied atmospheric pollution in Salford and reported concentrations of 3:4 benzpyrene of 20 to 25 ug per 100 cubic meters. In Sheffield on three foggy days it has been as high as 32.8 ug per 100 cubic meters. Stocks and Campbell (1955), gave figures of up to 8.5 ug per 100 c.m. They state that the average man breathing 20 cubic meters a day would have an intake of 1.2 ug. This is equal to the content of over 100 cigarettes, according to Cooper. A similar figure

is suggested by the Tobacco Manufacturers Committee (1957), from their laboratory findings, namely that the daily intake of benzpyrene from breathing London air is equivalent in total volume to the intake from smoking about 100 cigarettes a day. If we take the figures for Sheffield quoted above; the amount of benzpyrene breathed in in one day might be, prima facie, equal to the content of 600 cigarettes.

However, Cooper, Lindsey, and Waller (1954), consider that the 3:4 benzpyrene in the atmosphere is likely to be less active biologically than the carcinogens in cigarette smoke which contains powerful solvents such as pyridine. The burning cigarette may attain temperatures up to 900°C. and the main body of the hot end is always at a temperature of between 650 and 700°C. These temperatures are sufficiently high for pyrolysis of simple compounds to polycyclic hydrocarbons. Perhaps in addition to arsenic, azulene, anthracene, pyrene, acenaphthylene, and 3:4 benzpyrene there are other hydrocarbons with a short fleeting existence, produced by the burning cigarette.*

Atmospheric soot is produced largely from chimney smoke, motor and diesel engines and railway engines. One of the major sources of pollution is the domestic fire, but we have been exposed for so long to atmospheric pollution by domestic smoke that this factor is unlikely to be the sole cause of the recent recorded increase in cancer of the lung.

Petrol and diesel engine exhausts have a relatively low content of benzpyrene (Editorial Brit. Med. J., 12.5.56; Fitton 1956), and there does not appear to be any excess

* More recently Dr J.W. Cook (Med. Officer II p171, 20.9.57), has described the presence in cigarette smoke of the active carcinogen 3:4-9:10-dibenzpyrene in perhaps significant quantities, as well as radio active potassium in probably insignificant quantities.

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incidence of lung cancer among persons exposed such as Metropolitan policemen, bus drivers, or tractor drivers. Kotin et. al. (1954), did extensive work on exhaust fumes in Los Angeles where the consentration of automobiles is high, and they attribute the benzpyrene in the atmosphere to this source. Later (1956), Kotin suggested that aliphatic materials from incompletely burned petroleum fuels by oxidation and chain reactions might lead to the production of agents capable of eluting adsorbed carcinogens from smoke particles following their deposition on the respiratory mucosa.

There is now a large amount of statistical evidence regarding the relative mortality from lung cancer of smokers and non smokers. About twenty studies seem to confirm a statistically significant excess of the disease among the smokers.

Doll and Bradford Hill (1956), consider that the relationship holds only for the epidermoid and anaplastic cancers (including the oat-cell type), and only to a lesser degree, if at all, to adenocarcinomes.

Generalising they conclude that if the annual death rate for non-smokers is reckoned as unity, the rate for smokers of 1 to 14 cigarettes a day will be 13; for smokers of 15 to 24 cigarettes a day it will be 24; and for smokers of over 25 cigarettes a day it will be 40.

The mortality was substantially less among pipe smokers in each equivalent category.

Lung cancer of course occurs among non-smokers but not very often among males. It has however been estimated that only a very small percentage of heavy smokers develops lung cancer perhaps up to 4%.[x] Nor does there seem to be any excess of the disease among those smokers who inhale deeply. Again, in the present series at least, (see Table 27), there did not seem to be any pattern connecting the patients age at the onset of the disease with the amount smoked and the number of years he had been a smoker.

No useful figures were obtainable regarding the urban: rural incidence of lung cancer in my study. Figures generally are complicated by the fact that smoking is more prevalent in the towns than in the country. Historically also the death rate from all causes has always been greater in urban than in rural populations.

Doll and Bradford Hill (1956), consider that there is a 2:1 mortality ratio from lung cancer between town and country dwellers.

Lew (1955), demonstrated a 30 to 50% urban:rural difference in lung cancer among male clients of the Metropolitan Life Insurance Company.

Eastcott (1956), considered the higher incidence of lung cancer among immigrants than among the native New Zealanders to be related to previous residence in industrial areas.

Ch. 15 : P. 26

x Figures up to 12.5% (1 in 8) have been suggested for males over the age of 50 smoking over 20 cigarettes a day. (Clinical Excerpts - Bayer - 1957. Vol. XXXIX).

Stocks and Campbell (1955), state that the urban:rural mortality ratio falls progressively from about 9 to 1 among non-smokers to a small value approaching unity among heavy cigarette smokers. This could support the theory that atmospheric pollution may be of aetiological importance.

Haenszel and Shimkin (1956), state that in the U.S.A. deaths from bronchial carcinoma for 1950 gave an urban:rural ratio of from 1.63 to 2.84 for males and from 1.24 to 1.60 for females. The ratio for women was rather less than that found by British workers and was smallest among non-smokers, which is slightly against the atmospheric pollution theory.

4. HORMONE DEPENDENCY.

As stated in Chapter 14 no positive findings were obtained from such enquires as I could make regarding the endocrine balance of the cases of bronchial carcinoma. For the sake of completeness however I would like to mention some facts regarding this line of approach.

Lacassagne in his studies on breast cancer in mice in 1932 discovered that the naturally occurring oestrogenic steroid hormone oestrone was implicated. The terms hormone-dependent and hormone-independent cancers were first used by Huggins of Chicago in 1945. About 50% of human carcinomas of breast and prostate seem to be initially hormone-dependent.

Kennaway (1955a), points out that Doll (1953a), considered that about one fifth of the 15,000 annual deaths from bronchial carcinoma at that time i.e. about 3,000, were not due to tobacco, and considers the study of this group as very valuable.

In it there appears to be an absence of any sexual difference and a lack of correlation with density of population, which suggests an intrinsic factor of causation. If this factor has not altered during the last 30 years Kennaway considers one must assume that the accepted total of 612 cases of lung cancer for 1922 was inadequate. It would be interesting to know the peak age incidence and predominant histology of this group.

Cade (1955), speaking of mammary and prostatic cancer states that "cancer is not necessarily, as previously thought, always an autonomous and self-perpetuating disease, but is dependent on its hormonal enviroment. The most urgent need at present is for accurate laboratory methods to estimate various hormones".

It is well known that the rate of growth of tumours varies widely and this cannot always be explained on anatomical or histological grounds.

Green (1953), transferred human lung cancer direct from the operating room to the eye and brain of experimental animals and found the tumours capable of growth in all instances. By contrast the majority of breast cancers were in a dependent phase and not transplantable at the time of first surgical approach.

The uniformity of success in the transplanation of bronchogenic carcinoma may be caused by its rapid development from dependency to autonomy, or to the advanced stage of most lung cancers at the time of clinical recognition. Perhaps clinical recognition is preceded, in most cases, by a silent period of some duration.

5. EARLY DIAGNOSIS AND THE SILENT PERIOD

As stated in Chapters 9 and 10, neither a short history nor relatively slight X-Ray changes are necessarily associated with freedom from metastases on diagnosis. When we consider also, that a third of the male cases at any rate, have been suffering from chronic chest disease prior to the onset of the carcinoma it seems that EARLY DIAGNOSIS IN MOST CASES OF CANCER OF THE LUNG DOES NOT SEEM TO BE OBTAINABLE WITH THE MEANS AT OUR DISPOSAL AT PRESENT.

In this series, as stated in Chapter 6, the resection rate was 11%. This figure is fairly general and attempts to increase it have been achieved only by accepting more advanced cases.

Nicholson (1957), found that his operated cases gave an average history of symptoms of six months.

Overholt and Schmidt (1949), estimated that the average patient waits three months before seeking advice and that another seven months is lost in medical observation.

In this series the average duration of the period Chest Clinic to Surgeon was four weeks with the exception of one case (see Table 21). In four other cases not referred to the surgeon there seemed to have been a delay on the part of the Chest Clinic or M.O.P.D. of over four months (Table 21). In one of these cases the delay was due to the patient failing to keep appointments. In the other three cases had it not been for the delay operation might have been a possibility. ×

In addition to these cases four patients refused operation.

The average period between the patient seeing the surgeon and operation was three weeks.

There is probably a delay for a month or two on the part of most patients before going to their doctor and again by the doctor before referring them for investigation. Better case taking and a greater awareness of the various atypical syndromes of the disease may lead to a very few more cases being discovered in an operable stage. The resources of Mass Radiography should be used wherever possible.

As a corollary of the tragic fact that 75% of cases are inoperable on first diagnosis can we assume that a silent antecedent period of some duration exists? This is perhaps the most facinating and hopeful aspect of the disease, because in it, in the future, some therepeutic action may become possible along the lines hinted at by Sir Stanford Cade (P.187).

The reasons advanced in support of the existence of an antecedent pre-clinical silent period are listed as follows:-

× Two additional cases initially diagnosed as tuberculosis are described on pages 20 (Bonfiet 270) and 25 (Van Hessel 271)

1. Silent X-Ray changes found by chance.

Rigler et al. (1953), studied the duration of illness on the basis of previous X-Ray examinations, and found that while in 37 inoperable patients the average duration of symptoms was 12.7 months, X-Ray signs had preceded the onset of symptoms by 7.8 months. In 13 operable cases, the average duration of disease as determined by X-Ray signs was 36.4 months.

In a small series such as the present only a few cases changed to have been X-Rayed before. However in six patients previous X-Rays were obtained and were thought to show early changes that represented the subsequent carcinoma. These had been taken 4 years, 3 years, 2 years, 18 months, 16 months and 10 months before symptoms arose.

Rosenblatt and Lisa (1956c), on the basis of retrospective studies, suggest a latent symptomless period of several years.

Overholt and Schmidt (1949), reported a case in which an abnormal X-Ray shadow was observed for nine years. At operation a resectable bronchial carcinoma was found.

White et al. (1952), reported a case of 11 years duration who lived 4 years after palliative surgery.

It is of course possible for such cases to be confused with carcinomas arising in relation to previously existing tuberculosis or post-infective scars or cysts.

2. Bronchoscopic studies also have suggested the existence of a silent period. Thus Mitchell (1955), described six, otherwise symptomless, cases of haemoptysis who

had clear X-Rays but positive bronchoscopic evidence of carcinoma. One of these cases felt well and had coughed up the blood at work. At thoracotomy, however, the disease was already inoperable and he died within three months.

3. The primary lesion may be minimal while extensive silent metastases are taking place. Such a case is described in Chapter 7, P.75, (Gillibrand-115). This is the main reason why early diagnosis is so difficult if not impossible.

In this series, as described in Chapter 9, it is estimated that 70 to 80% of the cases may have had metastases on first diagnosis, and that in 50% of the cases the first symptom that made them go to their doctors was due to a metastasis.

4. It is possible, although cancer of the lung is always in a hormone - independent phase by the time operation is carried out, that like cancer of breast and prostate it goes through an early, pre-clinical, silent, hormone-dependent phase.

5. The "silent period" may be similar to the intermission period following operation on a cancer before recurrence sets in. Thus Temple (1957), described a recurrence in the bronchial stump nine years after lobectomy. One may in such a case be excused for presuming that the recurrence was of the original lesion. Yet during these nine years its growth was very slow or spasmodic.

One may perhaps therefore consider the life history of the disease to be like an iceberg with the silent period representing the volume below the water. Also under the water is the

small growing primary lesion and perhaps a slight X-Ray shadow, and possibly some slight bronchoscopic change and even silent metastases.

A diagrammatic representation of a hypothetical silent period and four possible courses of the disease growing out of it has been attempted in Fig. 13.

Four hypothetical courses of the disease are represented in Fig. 13 as aA, bB, cC, and dD.

In the course aA, either there is a long silent period or the growth is rapidly extending. By the time symptoms and signs appear metastases are present and death soon supervenes. I would put 65% of ~~the~~ my total cases in this class.

In the course represented by bB the patients already had very early metastases on diagnosis, and were inoperable but quite well physically and they survived for up to ~~two~~ three years. This group is estimated at 15% of all cases. If this group is referred early enough after the onset of symptoms there might be a very small chance for surgical treatment.

In the course represented by cC, estimated at about 10% of cases, spread to local mediastinal glands has taken place but the patient is usually fit for thoracotomy, and perhaps for resection.

The course represented by dD represents the operable cases free from metastases on diagnosis. This group is estimated at approximately 10%.

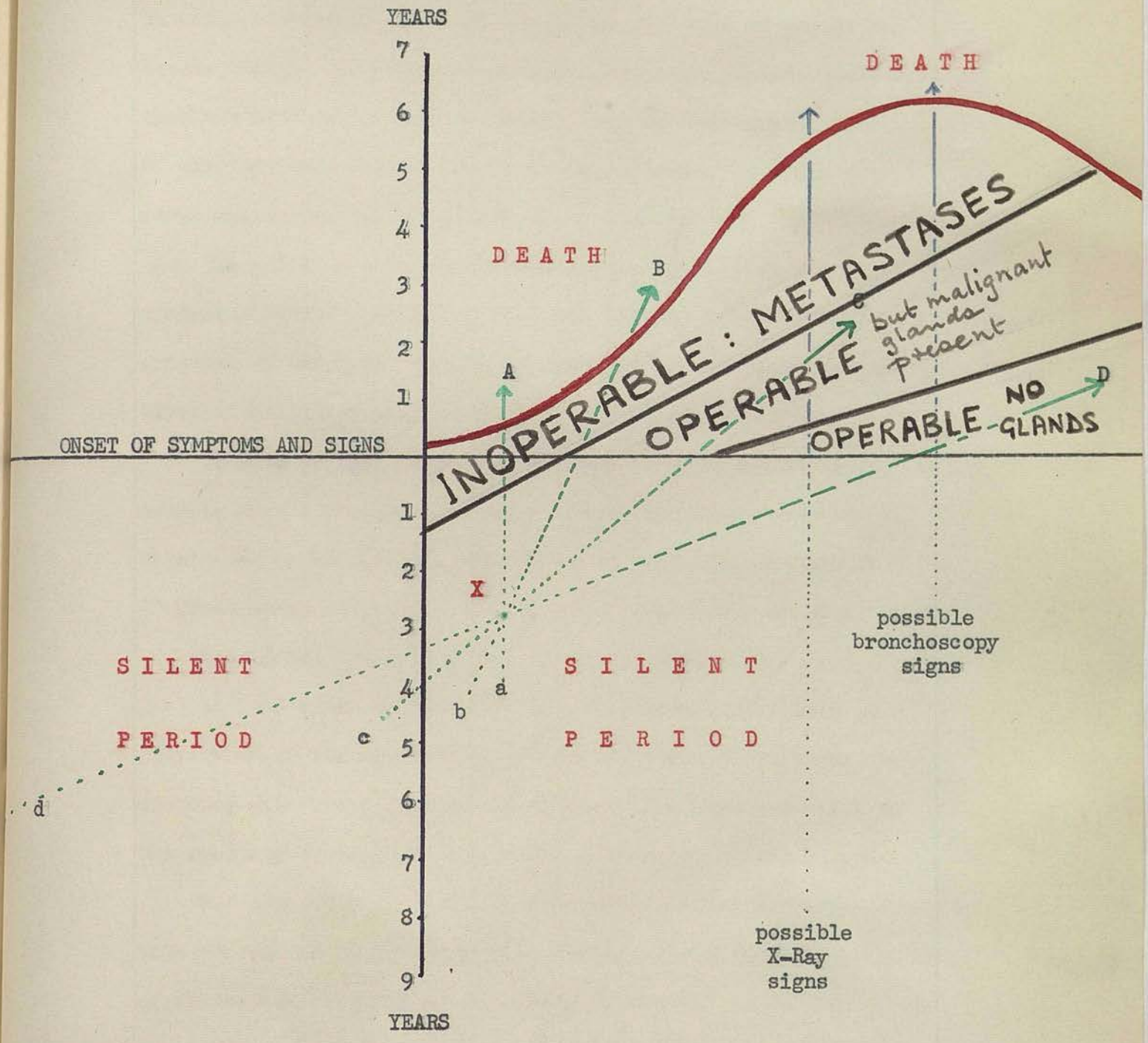

FIG. 13. - Diagrammatic representation of a hypothetical 'silent period', and four possible courses of the disease, aA, bB, cC, and dD.

The rate of growth of the carcinomas may not, of course, be a simple progression but may become progressively faster. In untreated cases one would not expect the rate of growth to become slower, therefore ~~the rate of growth to~~ one has presumed that the differing rates of growth observed during the period of clinical observation are paralleled between the different cases during the silent period.

The point in the life history of the disease at which diagnosis takes place is so variable, and the duration of symptoms so difficult to assess, that individual cases of all types of histology will probably be found in each group.

In Fig. 13 the lines representing the four hypothetical courses of the disease have been made to intersect at point X within the silent period, thus assuming that the operable case dD grows most slowly, and the others progressively faster.

Reasons for supposing this to be the case are:-

1. As shown in Table 10, (P. 67), there is a high proportion of the more slowly growing squamous cases among the operated cases free from glands and the five year survivors of the operated cases free from glands (Table 16, P. 89).

2. The average duration of symptoms before diagnosis in this series was longer for the operated cases without involvement of the mediastinal glands than for the operated cases with involvement of the mediastinal glands. It was also longer for all the operated cases than for the non-operated cases (Table 18, P. 93).

Lindskog and Bloomer (1948), found the duration of symptoms longer in the resectable than in the non-resectable cases.

Gifford and Waddington (1957), found, like Bignall and Moon (1955), that the best chance of survival was among those with a long history of over nine months.

3. The cases with the shortest history and survival period were those admitted to hospital in a preterminal state and subjected to diagnostic necropsy (Table 25, P. 136). In these cases an excess of quick growing anaplastic lesions is to be expected, (Table 16, P. 89). Similarly anaplastic cases generally, and cases among younger adults, (Table 14, P. 84), appear to grow quickly and have a shorter history and a short survival period. All these cases seem, more or less, to follow the path aA in Fig. 13.

4. As shown in Table 14, (P. 84), the longest duration of symptoms is found with the longest survival period among the squamous cases, and the shortest duration of symptoms is found with the shortest survival period among the anaplastic cases.

As shown in Table 21, (P. 107), of the 31 cases with a known history of possibly over two years the histology was known in 12 cases. Nine of these were squamous and five of these were operated on. Three were anaplastic, their average survival period ~~was~~ being only 8 weeks.

That a silent period of up to say 18 months exists seems fairly certain. Periods up to 10 years have been suggested. Whether the anaplastic types have as long a silent period seems doubtful and we cannot say how long before the onset of symptoms one might place point X in Fig. 13, perhaps only a few months.

During the silent period although metastases may be taking place the process cannot in most cases be revealed by X-Rays. It may be therefore that the cases at present being operated on are just a few of the slower growing group that happen to be free from metastases and to which attention has been directed by a chance X-Ray or early symptoms connected with the primary growth.

Among the anaplastic group and indeed among most of the squamous group early diagnosis cannot compensate for their rapid metastatic spread during the silent period.

Perhaps in the future ways will be found, for example by biochemical tests or hormone-assay, of studying operated cases, or even of diagnosing new cases during the silent period.

6. CANCER NOTIFICATION AND REGISTRATION

If it could be shown that cases would be found earlier, this would be a very strong argument in favour of cancer notification.

The main delay, if any, appears to be either on the part of the patient himself or his General Practitioner. Compulsory notification might induce the latter to refer more cases, even vaguely suspicious cases, to the chest clinic or hospital. It

seems unlikely that notification would improve the speed of disposal from the chest clinic or hospital to operation although it might enable physicians to seek surgical advice sooner.

With the present low general level of confirmation of diagnosis, it seems unlikely that universal notification would increase the amount of accurate scientific knowledge available for research purposes, unless it were linked with a high degree of histo-pathological verification.

This point was stressed by the Council of the International Organisations of Medical Sciences (under the joint auspices of W.H.O. and U.N.E.S.C.O.), (Clemmeson 1954). The council also drew attention to the necessity for the correct use of the International Statistical Classification of Diseases and to the need for a simple histological classification with reference, where necessary, to the International Manual of Tumour Nomenclature and Coding.

Stocks (1950), gives a history of Cancer Registration in England and Wales.

The Radium Commission from 1930 kept records at Radiotherapy Centres.

In 1939 the Cancer Act required the Council of every County and County Borough to arrange facilities for treating cases in their area. The Ministry advised the Councils that they should send copies of records of treatment and its results to a person designated.

In 1944 the Ministry issued a circular letter to the authorities, together with specimens of Registration and Case Abstract Cards which were prescribed as from October 1st, 1944, for use in all areas where a cancer scheme, which had been approved by the Ministry, was operating.

At the end of the war the Radium Commission introduced a similar system of record cards in its radiotherapy centres.

In June 1945, the Commission was nominated temporarily as the Statistical Bureau for the collection and analysis of records, and this duty was taken over by the General Register Office in 1947.

When the National Health Service Act came into force in July 1948, the Cancer Act was repealed, and the continuation and extension of the plan for cancer records became the business of the Regional Hospital Boards and Boards of Governors.

By 1955 registration was only 55% complete over the whole of England and Wales, though even this figure provided the largest number of cases of cancer in the world registered on a uniform system.

Notable contributions have been made by Vick of the South-Western Regional Hospital Board (1955) and by the Liverpool (1954), and Oxford Boards (Barr 1957).

For every case of suspected malignant disease coming under treatment a Registration Card is filled in by the centre at the end of the month and sent to Somerset House. An Abstract Card is sent later giving the diagnosis, treatment, and histology. Each case is followed up for twenty years, and,

in addition, the date and cause of death of any registered cancer patient is notified back to the registering centre by the General Register Office.

Two important studies on the results of treatment Stocks (1950), and H.M.S.O. (1952), have already been published.

CHAPTER 16

PRECIS

Most statistical reports relating to primary lung cancer have come from surgical centres or special clinics and have been previously selected to a varying degree.

In order to compare the operated and non-operated cases, assess the proportion operated on, the percentage verified histo-pathologically, the accuracy of the diagnosis and death certification, the state of the average patient on first diagnosis, and the survival periods of the different groups, an attempt has been made to study every case occurring in one area in one year.

Every case of bronchial carcinoma first diagnosed in the geographical area of the Blackburn and District Hospital Management Committee during 1955 has been studied and followed up.

The population of this area is 271,870, and the number of cases occurring was 123, (102 male, 21 female). My incidence figures are therefore 45 per 100,000 (81 per 100,000 for males, and 14 per 100,000 for females).

One sixth of the cases had been initially referred to the Chest Clinics. Half of the remaining five-sixths were referred to general hospital out-patient departments and half were admitted direct as general hospital in-patients.

The average age of the male cases was 61 years, of the female cases 63 years.

Special care has been taken to give statistical figures for the non-operated as well as the operated group.

In addition to the 123 cases of bronchial carcinoma, another 131 observation cases, in whom the diagnosis was rejected, have been studied to illustrate diagnostic problems, and to assess the probable accuracy arrived at.

Of the 123 carcinoma cases only 49 (40%) were confirmed histologically, (only 37% during life). Another 17 were confirmed pathologically (mostly at p.m.). Another 21 were accepted as free from doubt on the basis of clinical and X-Ray evidence, but in the remaining 36 cases a varying degree of doubt existed as to the certainty of the diagnosis.

After considering these cases and the 131 rejected observation cases in detail, a probable diagnostic error of ± 10% or more, is suggested.

Of the 127 bronchoscopies done, 42 were on the 131 observation cases for diagnostic purposes, and 85 on the 123 carcinoma cases. These 85 examinations were, however, on only 61 individuals, 40 of whom gave positive visual evidence and 32 a positive biopsy. This represents a positive biopsy in only 26% of the total 123 cases, or a positive histological finding in only 1 in 4 of the bronchoscopies done. The bronchoscopy cases were younger and fitter than the average.

Fourteen cases, 13 male and 1 female, making 11% of the total, had a thoracotomy, and 13 cases or 10% had a resection. Seven of these had no evidence of secondary deposits in the regional glands, representing 54% of the operated cases, but only 6% of the total cases. Of these 7 cases, 5 are alive,

all well and working after two years. Of the 6 cases with mediastinal glands at operation only one is alive and he is ill. The average age of the operated cases was 54 years, compared with 61 yrs. for all cases.

Four cases otherwise fit refused surgery. All the 110 non-operated cases are now dead except three who are all very ill.

Of the deaths, 63% occurred at home and only 37% in hospital. Of the 42 cases dying in hospital necropsies were carried out on 18 i.e. on 43% of those dying in hospital, but on only 16% of the total deaths.

The necropsies were divided quite sharply into two groups:

1. Those done for diagnostic purposes on old ill patients with acute disease.

2. Those done on hospital readmissions out of interest.

In only 49 patients (40%) was the histology known. This was discovered as follows:- bronchoscopy biopsy 32 cases, operation histology 13 cases, necropsy histology 5 cases, sputum cytology 3 cases, thoracotomy 1 case, and biopsy four cases (2 glands, 1 abscess, 1 skin). Of these 49 cases there were 30 squamous (female 4), 5 adenocarcinomas (female 1), and 14 undifferentiated (female 3). Only 6 of these 49 patients are alive after two years, four squamous cases and two adenocarcinomas. None of the undifferentiated cases are alive.

Taking my series along with several larger series one finds a gradual increase in the proportion of squamous cases, and a corresponding reduction in the proportion of undifferentiated cases in the following groups:- necropsy, unfit

operation, total cases, operated cases, and 2, 3, and 5 year survivors. The percentage of squamous cases varies from 21% of some necropsy series to 91% in one series of operated 5 year survivors.

The difficulties of obtaining histological verification are discussed. Admitting them to be formidable, however, a plea is made for a study, such as the present, but with full histological backing, to define the true overall incidence of each histological type in every case in one area over a certain period of time, and so in bronchial carcinomas as a whole. Only when this has been done can we assess the real chances of early diagnosis and the true scope of surgical treatment.

Estimations of the duration of symptoms before diagnosis are unreliable. The average was 7 months but in 31 cases continuous symptoms seemed to go back two years or more.

The duration of symptoms and signs is no certain guide to operability. About 80% of cases were thought to have evidence of metastases on first diagnosis. Out of 13 known anaplastic cases 12 were thought to have secondaries on first diagnosis. In more than 50% of cases the first symptom that made the patient go to his doctor was due to the presence of a metastasis.

Some tentative classifications of the X-Ray pictures has been attempted in relation to bronchoscopic appearances and operability and survival. The best prognosis was associated with coin shadows, then with cases showing linear streaking or

pneumonitis, segmental collapse, dense hilar shadows and lobar or massive collapse in that order.

In 19 cases a pleural effusion was present on first diagnosis; eight of these were females. The criteria of diagnosis of this group was poor. The average survival period was only 12 weeks, with the exception of one case (Fig. 9 : P. 120), who in spite of a long history and a large effusion was successfully operated on. He is now well and working.

The total 123 carcinoma cases gave a 7.5% two year survival rate, of which the 13 operated cases made up 5%, and the 110 non-operated cases 2.5%. There is however more disparity between the two groups than these figures suggest, 5 of the 6 operated survivors being well and working while all the three non-operated survivors are very ill.

A third of the non-operated cases were dead within 5 weeks of diagnosis, half within 8 weeks and three-quarters in 6 months.

After about 14 months the 8 survivors of the 13 operated cases outnumbered the 7 survivors of the 110 non-operated cases. Among the operated group the two year survival rate was 50%. The outcome of operation appears to depend chiefly on whether or not the regional glands are involved.

Various groups of the cases are tabulated in Table 25 (p. 136), and their survivors and average survival periods shown. Generally speaking all the operated groups (except the undifferentiated), including those with nodal involvement, and all cases free from metastases on diagnosis, and even the

age group 46 to 60 taken as a whole, did better than the average for all the 123 cases.

On the other hand, undifferentiated cases, whether operated on or not, cases with metastases on first diagnosis, cases with an effusion, female cases generally whether operated on or not, and all cases in the age groups under 46 and over 60, seemed to do less well than the average.

The survival periods of individual cases showing various symptoms and signs such as hoarseness, dysphagia, paralysed diaphragm and liver enlargement are recorded in Table 18, P.93.

The estimated diagnostic error of ± 10% or more, is passed on to the death certificate. The use of the clinico-pathological classification of the C.I.O.M.S. (Clemmesen 1954), is strongly recommended, and certain slight modifications to this classification are suggested. It is also suggested that it might be possible to incorporate this classification in the death certificate to show which of the three degrees of certainty applied. In my opinion cancer of the lung should never be diagnosed on the grounds of history and clinical findings alone.

Among the 102 male cases there were no non-smokers and indeed no cases smoking less than 10 cigarettes a day (excluding 2 cases who smoked pipes only). There were only 20 male cases smoking less than 20 cigarettes a day.

Among the 21 female cases there were seven non-smokers. Figures are given from recent surveys which suggest that the smoking habits of my cases, both males AND FEMALES are in excess of those of the general population of similar age and sex.

Thirty-one cases gave a continuous history of chest illness for an average of 14 years before the onset of the carcinoma. It was not possible to assess the point when these symptoms first became related to the carcinoma. In addition another 16 cases gave a history of chronic chest symptoms (perhaps slight) for many years. Another 23 cases gave a definite history of a short period acute chest illness.

Of the 102 male cases 60 were exposed to considerable smoke or fumes at work, but only one of the 21 female cases was so exposed.

In the discussion the various changes in the International Classification of the disease are described and absolute death figures are given. These rose from 3000 in 1925 to 18185 in 1956 in England and Wales, bronchial carcinoma now being the sixth single cause of death after heart disease, alimentary cancer, pneumonia, bronchitis and violence. The actual figures for the deaths from bronchitis, pneumonia, influenza, respiratory tuberculosis, and the "senility and ill-defined causes" group are given year by year from 1925 to 1955. Over these 30 years the deaths recorded every year from these causes has fallen by 75,000. That this has increased the

bronchial carcinoma list seems likely but does not exclude the possibility of a real increase.

The increased incidence of the disease has been more marked in men than in women; possible reasons for this are discussed.

A short résumé is then given of the literature relating to carcinogens and the relationship of the disease to smoking and atmospheric pollution.

The possibilities of early diagnosis are discussed. Because of silent metastases there does not appear to be any easy answer to this problem. Evidence, however, is collected relating to the possible existence, in some cases, of a considerable SILENT PERIOD - perhaps of some years duration, prior to the onset of symptoms and clinical signs, during which X-Ray changes may be present. Perhaps in the future this period will be able to be exploited from the diagnostic point of view, by biochemical or other means.

Finally a short description is given of cancer registration.

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